Blood Lead Levels in the US Population

Phase 1 of the Third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1991)

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Objective.—To determine mean blood lead levels and their sociodemographic correlates in the US population.

Design.—Nationally representative cross-sectional health examination survey that included measurements of venous blood lead.

Participants.—A total of 13 201 persons aged 1 year and older examined during phase 1 of the third National Health and Nutrition Examination Survey (1988 to 1991).

Results.—The overall mean blood lead level for the US population was 0.14 µmol/L (2.8 µg/dL). Blood lead levels were consistently higher for younger children than for older children, for older adults than for younger adults, for males than for females, for blacks than for whites, and for central-city residents than for non–central-city residents. Other correlates of higher blood lead levels included low income, low educational attainment, and residence in the Northeast region of the United States. National estimates for children 1 to 5 years of age indicate that 8.9%, or approximately 1.7 million children, have blood lead levels 0.48 µmol/L (10 µg/dL) or greater. These levels are high enough to be of health concern under 1991 Centers for Disease Control and Prevention guidelines.

Conclusions.—The low overall mean blood lead levels demonstrate a major public health success in primary prevention efforts. However, exposure to lead at levels that may adversely affect the health of children remains a problem especially for those who are minority, urban, and from low-income families. Strategies to identify the most vulnerable risk groups are necessary to further reduce lead exposure in the United States.

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THE PERSISTENCE of lead in the environment poses an ongoing challenge to the field of public health. A toxicant whose deleterious health effects have been known since antiquity, lead continues to attract national attention. The pervasiveness of lead is illustrated by reports of sources of exposure that range from paint removed during the renovation of a Victorian farmhouse[1] to contaminated soil concentrated in urban play areas[2] to traditional medicine ingested for a stomach ailment.[3]

Strategies to eliminate lead poisoning include reducing sources of exposure, increasing safe and effective abatement programs, and identifying persons at risk.[4] Surveillance plays an important role in documenting lead exposure by characterizing vulnerable population groups and assessing the effectiveness of intervention efforts. Blood lead levels measured as part of the National Health and Nutrition Examination Surveys (NHANES) conducted by the National Center for Health Statistics/Centers for Disease Control and Prevention (NCHS/CDC) have contributed to the national surveillance of lead exposure in the United States. The NHANES provide blood lead level estimates for population subgroups by age, sex, race/ethnicity, income level, urban status, and region of the country. The second National Health and Nutrition Examination Survey (NHANES II, 1976 to 1980) yielded the first national estimates of blood lead levels.[5] Estimates were also produced from the Hispanic Health and Nutrition Examination Survey (1982 through 1984), a special survey of Mexican Americans, Cubans, and Puerto Ricans.[6]

See also pp 284 and 315.

This article presents blood lead levels from phase 1 of the third National Health and Nutrition Examination Survey (NHANES III phase 1, 1988 to 1991), the most recent of the NHANES. The distribution of blood lead levels is described by sociodemographic characteristics for persons aged 1 year and older. A new feature of the survey was the extension of sampling to persons older than 74 years, which enabled the determination of blood lead levels in the growing subgroup of older Americans.

METHODS AND PROCEDURES

NHANES III Sample Design

The NHANES III, a 6-year survey measuring the health and nutritional status of the civilian noninstitutionalized US population aged 2 months and older, is being conducted by the NCHS/CDC from 1988 to 1994. National population estimates as well as estimates for the three largest race/ethnicity subgroups in the US population (non-Hispanic white, non-Hispanic black, and Mexican American) can be derived from each of two individual 3-year phases or from the full 6-year survey. Phase 1 was conducted from October 1988 through October 1991.

The sampling scheme for NHANES III was based on a complex multistage area probability design. Children younger than 5 years, adults aged 60 years and older, blacks, and Mexican Americans were

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oversampled. A detailed description of the sample design has been published.[7]

Data were collected through a household interview and a standardized physical examination conducted in a mobile examination center. Sociodemographic information and medical histories of the survey participant and the family were collected during the household interview.

Laboratory Methods

During the physical examination, a 1-mL sample of ethylenediaminetetraacetic acid–anticoagulated whole blood was obtained by venipuncture from participants aged 1 year and older. Blood specimens were frozen and shipped on dry ice to the NHANES laboratory, Division of Environmental Health Laboratory Sciences, National Center for Environmental Health, CDC, Atlanta, Ga, for analysis. Specimens remained frozen at –20°C until analysis.

Lead was measured by graphite furnace atomic absorption spectrophotometry (GFAAS) using the method of Miller et al.[8] The lead content was determined using GFAAS with deuterium background correction (Perkin-Elmer Model 5000). This method has been optimized for sensitivity at lower blood lead levels resulting in a detection limit of 0.05 µmol/L (1.0 µg/dL). In all statistical analyses, blood lead levels less than 0.05 µmol/L (1.0 µg/dL) (6.5% of the samples) were assigned a level of 0.02 µmol/L (0.5 µg/dL).

Analysis of each specimen was performed in duplicate, and the mean of the duplicate measurements was reported. All specimens containing lead concentrations greater than 0.72 µmol/L (15 µg/dL) or less than 0.07 µmol/L (1.4 µg/dL) were rediluted and reanalyzed by GFAAS for confirmation. A comparison between GFAAS and inductively coupled mass spectrometry showed good agreement at very low concentrations of lead.

Bench and blind quality control (QC) procedures were used to assure quality of the lead analyses.[9] Four bench QC samples were inserted in each run of 60 specimens to evaluate method performance on the day of analysis. In addition, 5% of the samples were blind QC samples, which appeared as a regular unknown sample to the analyst. Blind QC results were monitored by a scientist not involved in the analysis of samples. The QC results showed no statistically significant trends in blood lead level measurement during the 3-year study period of October 1988 through October 1991.

Demographic and Socioeconomic Covariates

Age was reported at the time of the household interview as the age in years at last birthday. Age categories used in analyses were 1 to 2 years, 3 to 5 years, 6 to 11 years, 12 to 19 years, 20 to 49 years, 50 to 69 years, and 70 years and older. In the regression analyses, the first two age categories (1 to 5 years) and the last two age categories (≥50 years) were collapsed.

A composite race/ethnicity variable, based on reported race and ethnicity, was created to define three major race/ethnicity groups: non-Hispanic black, non-Hispanic white, and Mexican American. Persons from other race/ethnicity groups were included in the overall blood lead estimates but not in the estimates stratified by race/ethnicity due to limited sample size.

Education was dichotomized as high school graduate or less than a high school graduate. For adults aged 20 years and older, the variable reflected the education of the examinee. For children and youths aged 1 to 19 years, the education of the adult reference person was used in the analyses. The adult reference person was defined as one of the persons in the household who owns or rents the home.

Income level was defined by the poverty-income ratio (PIR): the total family income divided by the poverty threshold for the year of the interview. Income included the total family wages, salaries, Social Security and retirement benefits, and any other earnings received during the 12 months prior to the interview. The poverty threshold, determined annually by the US Bureau of the Census,[10-12] is adjusted for family size. The PIR was used both as a continuous variable and a categorical variable, defined as low ($0<PIR<1.30$), mid ($1.30\leq PIR<3.00$), and high ($PIR\geq 3.00$). These categories were selected in part to be consistent with major government food assistance programs that use a PIR of 1.30 to determine eligibility.[13]

Urban status was defined by population size and place of residence. Population was dichotomized as 1 million or more or less than 1 million. The place of the residence was designated as within or not within the central city of a standard metropolitan area. Population and place of residence were combined to create a single urban indicator with three levels: population of 1 million or more and central city; population of less than 1 million and central city; and non–central city.

Region, defined by the US Bureau of the Census, describes the geographic area of the United States where the examinee resided based on the categorization of states as Northeast, Midwest, South, and West.

Response Rates and Potential Nonresponse Bias

The current analysis was based on data from examinees aged 1 year and older. Of the 19 103 persons aged 1 year and older selected for the survey, 16 341 (86%) were interviewed and eligible for an examination. Of those eligible, 14 870 (91%) were examined. Blood lead determinations were available for 13 201 of the eligible examinees, representing 89% of the persons examined and 69% of the persons selected for the survey. Young children and older adults were more likely to have missing lead values.

To determine the potential effects of differential nonresponse on mean blood lead levels, an analysis of persons with lead values and persons without lead values (but interviewed) was conducted with respect to major demographic characteristics (age, sex, race/ethnicity, education, region, PIR, household size, location of residence, urban status, and sex and marital status of the adult reference person) as well as other health risk factors (overall health status, age of house, season, ever tested for lead, and identified or treated for lead poisoning). For each variable, the observed mean blood lead level in the examined sample was compared with the expected mean blood lead level in the interviewed sample, after adjusting for that variable. Using a method described by Flegal et al,[14] it was assumed that no significant differential in mean blood lead level resulting from nonresponse was present if the observed estimate was within 10% of the expected estimate. An analysis was also conducted to examine the potential bias of prevalence of high blood lead levels as defined by two values: 0.48 µmol/L (10 µg/dL) and 0.72 µmol/L (15 µg/dL). No bias in the mean blood lead levels or in the prevalence of high blood lead levels due to nonresponse could be detected.

Within-Person Variation

The effect of within-person variation on the prevalence of elevated blood lead level (≥0.48 µmol/L [≥10 µg/dL]) was determined to further assess the reliability of the estimates. Large within-person variation can distort prevalence estimates by increasing the total variance of the distribution.[15] A sample of examination participants aged 6 years and older (n=1149) provided blood specimens on two separate occasions in NHANES III phase 1 that were analyzed for blood lead level. Following a method described by Sempos et al,[15] an adjusted prevalence estimate was calculated to evaluate the potential effect of within-person variation. The correlation between the two blood lead values was 0.94. Because the adjusted prevalence of elevated blood lead level (4.2%) differed little from the unadjusted prevalence (4.4%), it was not considered necessary to adjust for within-person variation.

Statistical Analysis

Statistical analyses were conducted using SAS.[16] Survey sample weights were used for all analyses to produce estimates that were representative of the noninstitutionalized civilian US population. SUDAAN,[17] a statistical software package that incorporates the sample weights and adjusts for the complex sample design of the survey, was used to calculate appropriate SEs.

Geometric mean blood lead levels were calculated by taking the antilog of the mean of $\log_{10}$ of the measured lead values. In this article, elevated blood lead level was defined as 0.48 µmol/L (10 µg/dL) or greater for persons of all ages. The definition was selected to be consistent with the lowest blood lead intervention level designated in the current CDC guidelines for preventing lead poisoning in young children.[18]

Multivariate linear regression analyses were performed to determine the relation between blood lead level and sociodemographic variables. Separate models were run for five age categories: 1 to 5 years, 6 to 11 years, 12 to 19 years, 20 to 49 years, and 50 years and older. Log_{10} lead was used as the dependent variable. Independent variables included sex, age (continuous), race/ethnicity, PIR, education, urban status, and region. Marital status and sex of the adult reference person, household size, age of house, and a number of interaction terms were also examined but not included in the final models because they did not significantly add to the fit of the models. Persons who had missing values for education (1.1%), PIR (10.5%), or urban status (2.4%) were not included in the regression models.

RESULTS

Mean Blood Lead Levels by Age

Geometric means and 95% confidence intervals of blood lead levels are presented by age category along with population estimates in Table 1. Among children and youths, the geometric mean was highest for 1- to 2-year-olds and lowest for youths aged 12 to 19 years. Among adults, mean blood lead levels were highest in the older age groups. The mean blood lead level of the oldest adults was almost as high as that of the youngest children.

Mean Blood Lead Levels by Sex, Age, and Race/Ethnicity

Geometric mean blood lead levels varied by sex, age, and race/ethnicity as shown in Figs 1 and 2. Variations by age were similar for males and females; however, males showed consistently higher mean blood lead levels than did females except at the youngest ages (1 to 2 years), in whom blood lead levels were similar (Fig 1). Beginning at approximately 12 years of age, sex differences in blood lead levels were pronounced, with mean blood lead levels of males being greater than levels of females by 0.05 to 0.10 µmol/L (1 to 2 µg/dL). Mean blood lead levels among non-Hispanic blacks were consistently higher than those of non-Hispanic whites, although the pattern of variability was similar for both groups (Fig 2). Mean blood lead levels of Mexican Americans were slightly higher than those of non-Hispanic whites until age 60 years. The largest differences between the three race/ethnicity groups occurred at younger than 10 years; blood lead levels of non-Hispanic black children were 0.07 to 0.10 µmol/L (1.5 to 2.0 µg/dL) higher than the blood lead levels of Mexican-American children and at least 0.10 µmol/L (2 µg/dL) higher than those of non-Hispanic white children. Blood lead levels of non-Hispanic blacks older than 50 years consistently exceeded the levels of non-Hispanic whites and Mexican Americans.

The difference in mean blood lead levels by race/ethnicity persisted when stratified by sex, particularly for males (Table 2). For females, differences in mean blood lead levels by race/ethnicity were comparable with those of males but not as pronounced. Among older males, the mean blood lead levels of Mexican Americans were similar to levels of non-Hispanic whites and were on the average 0.10 µmol/L (2 µg/dL) lower than levels of non-Hispanic blacks.

Table 1.—Weighted Geometric Means and 95% Confidence Intervals (CIs) of Blood Lead Levels for Persons Aged 1 Year and Older by Age Category: United States, 1988 to 1991

Age, y	No. Examined	Population Estimate, Thousands*	Geometric Mean, µmol/L (µg/dL)	95% CI, µmol/L (µg/dL)
1-2	925	7476	0.19 (4.1)	0.18-0.22 (3.7-4.5)
3-5	1309	11 165	0.17 (3.4)	0.15-0.19 (3.0-3.8)
6-11	1587	21 748	0.12 (2.5)	0.11-0.13 (2.2-2.7)
12-19	1376	27 293	0.08 (1.6)	0.07-0.09 (1.4-1.9)
20-49	4320	112 283	0.13 (2.6)	0.12-0.14 (2.5-2.8)
50-69	2071	42 802	0.19 (4.0)	0.18-0.20 (3.8-4.2)
≥70	1613	19 440	0.19 (4.0)	0.18-0.21 (3.7-4.3)
All	**13 201**	**242 207**	0.14 (2.8)	0.13-0.15 (2.7-3.0)

*US Bureau of the Census, *Current Population Survey*, 1990.

Prevalence of Elevated Blood Lead Levels (≥0.48 µmol/L [≥10 µg/dL])

The overall prevalence of elevated blood lead levels (≥0.48 µmol/L [≥10 µg/dL]) was 4.5% (Table 3). Children aged 1 to 2 years had the highest prevalence, and youths aged 12 to 19 years had the lowest prevalence. Among adults, those aged 20 to 49 years had a prevalence only half that of adults in the older age groups.

The proportion of children aged 1 to 5 years with elevated blood lead levels varied by race/ethnicity (Table 4). The prevalence of elevated blood lead levels among 1- to 2-year-old non-Hispanic black children (21.6%; SE, 3.1%) was 2.5 times higher than the prevalence among non-Hispanic white children (8.5%; SE, 1.7%) and twice as high as among Mexican-American children (10.1%; SE, 1.9%). The prevalence among non-Hispanic black children aged 3 to 5 years (20.0%; SE, 3.1%) was similar to that of younger non-Hispanic black children but considerably higher than the prevalence among non-Hispanic white children (3.7%; SE, 1.8%) and Mexican-American children (6.8%; SE, 1.4%) in the same age category.

The prevalence of elevated blood lead levels among children aged 1 to 5 years increased with decreasing family income (Table 5). The prevalence for children from low-income families (16.3%) was four times higher than the prevalence for children from high-income families (4.0%). Non-Hispanic black children from low-income families had the highest proportion of elevated blood lead levels (28.4%). Among children from mid- and high-income families, the variability in the prevalence of elevated blood lead levels by race/ethnicity was less pronounced.

The prevalence of elevated blood lead levels was higher for children living in more urbanized areas (Table 5). By race/ethnicity, non-Hispanic black children residing in central cities with populations 1 million or greater had the highest prevalence of elevated levels (36.7%), more than seven times the prevalence for non-Hispanic white children residing in noncentral cities. A high proportion of Mexican-American children residing in the most urbanized areas also had elevated blood lead levels (17.0%). It should be noted that comparisons of estimates across race/ethnicity were limited due to the small sample of non-Hispanic white children living in the most urbanized areas.

Among adults (aged 20 years and older) the variability in the prevalence of elevated blood lead levels by race/ethnicity was similar to that of children. The prevalence was higher for non-His-

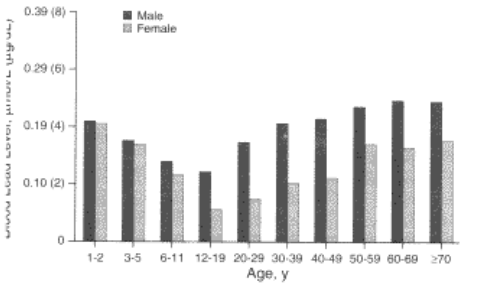

Fig 1.—Weighted geometric mean blood lead levels for persons aged 1 year and older by age and sex: United States, 1988 to 1991.

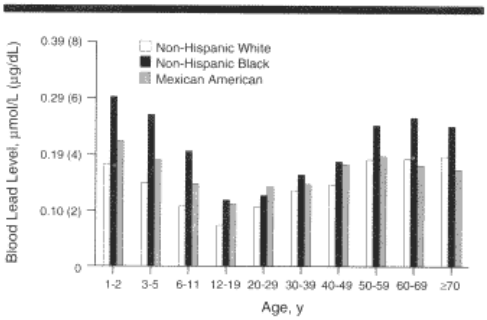

Fig 2.—Weighted geometric mean blood lead levels for persons aged 1 year and older by age and race/ethnicity: United States, 1988 to 1991.

Table 2.—Weighted Geometric Means and 95% Confidence Intervals (CIs) of Blood Lead Levels for Persons Aged 1 Year and Older by Age Category, Sex, and Race/Ethnicity: United States, 1988 to 1991*

	Non-Hispanic White			Non-Hispanic Black			Mexican American		
Age, y	No.	Geometric Mean	95% CI	No.	Geometric Mean	95% CI	No.	Geometric Mean	95% CI
					Males				
1-2	156	0.17 (3.5)	0.15-0.20 (3.1-4.1)	137	0.30 (6.3)	0.27-0.34 (5.6-7.2)	141	0.20 (4.2)	0.16-0.26 (3.3-5.3)
3-5	182	0.14 (2.9)	0.13-0.16 (2.6-3.2)	185	0.28 (5.9)	0.24-0.33 (5.1-6.8)	232	0.19 (4.0)	0.15-0.25 (3.1-5.1)
6-11	236	0.11 (2.4)	0.10-0.13 (2.1-2.7)	208	0.21 (4.5)	0.19-0.24 (3.9-5.1)	323	0.15 (3.1)	0.12-0.19 (2.4-3.9)
12-19	201	0.10 (2.1)	0.09-0.12 (1.8-2.5)	174	0.16 (3.2)	0.14-0.18 (2.9-3.7)	254	0.16 (3.3)	0.12-0.22 (2.5-4.4)
20-49	723	0.18 (3.8)	0.17-0.19 (3.6-4.1)	606	0.21 (4.5)	0.20-0.23 (4.2-4.8)	743	0.21 (4.4)	0.18-0.24 (3.8-5.0)
50-69	520	0.22 (4.7)	0.21-0.24 (4.5-4.9)	241	0.32 (6.6)	0.28-0.36 (5.8-7.5)	265	0.22 (4.5)	0.18-0.27 (3.7-5.4)
≥70	605	0.23 (4.8)	0.22-0.24 (4.5-5.1)	111	0.33 (6.8)	0.29-0.37 (6.0-7.6)	97	0.23 (4.8)	0.20-0.26 (4.3-5.4)
All	**2623**	0.17 (3.6)	0.16-0.18 (3.4-3.8)	**1662**	0.23 (4.7)	0.21-0.25 (4.4-5.0)	**2055**	0.19 (4.0)	0.16-0.23 (3.3-4.8)
					Females				
1-2	150	0.18 (3.6)	0.15-0.21 (3.0-4.3)	144	0.28 (5.8)	0.25-0.32 (5.1-6.5)	157	0.23 (4.8)	0.21-0.25 (4.4-5.3)
3-5	170	0.14 (3.0)	0.13-0.17 (2.6-3.5)	213	0.24 (5.0)	0.22-0.27 (4.5-5.6)	275	0.17 (3.6)	0.14-0.21 (3.0-4.5)
6-11	224	0.09 (1.9)	0.08-0.11 (1.6-2.2)	182	0.18 (3.8)	0.16-0.21 (3.3-4.4)	357	0.13 (2.8)	0.12-0.16 (2.4-3.3)
12-19	237	0.05 (1.0)	0.04-0.06 (0.8-1.1)	197	0.09 (1.8)	0.08-0.10 (1.6-2.0)	254	0.07 (1.5)	0.05-0.09 (1.1-2.0)
20-49	728	0.08 (1.7)	0.08-0.09 (1.6-1.9)	623	0.11 (2.2)	0.10-0.12 (2.0-2.5)	732	0.10 (2.0)	0.08-0.12 (1.7-2.5)
50-69	477	0.15 (3.2)	0.14-0.17 (3.0-3.5)	257	0.20 (4.3)	0.19-0.22 (3.9-4.7)	255	0.16 (3.2)	0.13-0.19 (2.7-3.9)
≥70	563	0.17 (3.5)	0.15-0.18 (3.2-3.8)	136	0.20 (4.2)	0.18-0.23 (3.7-4.7)	75	0.13 (2.7)	0.10-0.16 (2.1-3.4)
All	**2549**	0.10 (2.1)	0.09-0.11 (1.9-2.2)	**1752**	0.13 (2.8)	0.13-0.14 (2.6-3.0)	**2105**	0.11 (2.3)	0.09-0.13 (1.9-2.8)

*Geometric mean and 95% CI in µmol/L (µg/dL).

panic blacks than for non-Hispanic whites or Mexican Americans and generally increased with age (not shown). The prevalence of elevated blood lead levels for women of childbearing age was low. Only 0.5% of women aged 12 to 49 years had blood lead levels that were 0.48 µmol/L (10 µg/dL) or greater, and this prevalence differed only slightly by race/ethnicity.

Prevalence of Blood Lead Levels 1.21 µmol/L (25 µg/dL) or Greater

In 1991, the CDC lowered the blood lead intervention level for young children from 1.21 to 0.48 µmol/L (25 to 10 µg/dL).[18] As shown in Table 3, only a small proportion of the US population (0.4%) had blood lead levels that were 1.21 µmol/L (25 µg/dL) or greater. Children aged 1 to 2 years had the highest prevalence of blood lead levels 1.21 µmol/L (25 µg/dL) or greater, and adults aged 70 years and older had the lowest. By race/ethnicity (Table 4), the highest prevalence was observed for non-Hispanic black children aged 1 to 2 years (1.4%; SE, 0.7%).

Multivariate Regression Models

Coefficients from multiple linear regression models of the log of blood lead levels, stratified by age groups, are shown in Table 6. The variation in blood lead level described by the model (R^2) was similar in the first four age groups, ranging from .27 to .31 but was lower for adults aged 50 years and older (.16). Race/ethnicity was the only variable that significantly predicted blood lead level in all of the age-specific models. The size and direction of the coefficients for the other variables were consistent across most models, but the statistical significance varied by age. In general, sex (male), urban status (central city, ≥1 million), and race/ethnicity (non-Hispanic black and Mexican American) were associated with higher blood lead levels. The PIR (high) and education (at least high school) were associated with lower blood lead levels. Age was negatively associated with blood lead level in the three models describing persons aged 1 to 19 years. In the model for adults aged 20 to 49 years, age was positively associated with blood lead level.

The sociodemographic characteristics that were significant predictors of blood lead level for children and youth dif-

Table 3.—Percentage of Population Aged 1 Year and Older at or Above Selected Blood Lead Levels by Age Category: United States, 1988 to 1991

Age, y	Blood Lead Levels, %				
	≥1.21 µmol/L (≥25 µg/dL)	≥0.97 µmol/L (≥20 µg/dL)	≥0.72 µmol/L (≥15 µg/dL)	≥0.48 µmol/L (≥10 µg/dL)	≥0.24 µmol/L (≥5 µg/dL)
1-2	0.6	1.8	3.5	11.5	40.8
3-5	0.4	0.8	2.3	7.3	28.6
6-11	0.2	0.5	1.2	4.0	16.9
12-19	0.2	0.3	0.5	1.6	8.7
20-49	0.5	0.6	0.9	3.3	21.0
50-69	0.3	1.0	1.8	7.0	34.9
≥70	0.1	0.1	0.8	6.3	38.8
All	0.4	0.6	1.1	4.5	24.1

fered only slightly by age group. Sex was not an explanatory variable among 1- to 5-year-olds but was a significant predictor of blood lead level among children and youths aged 6 to 19 years. Urban status was significantly associated with blood lead level for persons in the age groups 1 to 5 years and 12 to 19 years; among 6- to 11-year-olds, the trend was similar but not statistically significant. Income and region were both significantly associated with blood lead level for children through 11 years of age. Education of the adult reference person (less than high school) was associated with higher blood lead level in all three models. The results of these analyses indicate that for children aged 1 to 5 years, blood lead levels were highest for non-Hispanic black children from low-income families living in the central cities with population 1 million or greater. The mean blood lead level for this subgroup was 0.47 µmol/L (9.7 µg/dL) compared with 0.18 µmol/L (3.7 µg/dL) for all children aged 1 to 5 years.

Of the two adult models, the model for 20- to 49-year-olds was able to explain the greatest proportion of the variation (31%) in blood lead level, and all sociodemographic variables in this model demonstrated independent associations with the dependent variable. In contrast, the model for adults aged 50 years and older explained only 16% of the variation. Five variables (sex, race/ethnicity, PIR, urban status, and region) were significant predictors of blood lead level.

COMMENT

For the second time in the past two decades, data on blood lead levels were collected in a national survey designed to estimate the prevalence of disease and other health-related parameters in the US population. An overall geometric mean blood lead level of 0.14 µmol/L (2.8 µg/dL) indicates a substantial reduction in lead exposure since the last national survey (NHANES II, 1976 to 1980), in which the geometric mean was 0.62 µmol/L (12.8 µg/dL),[5] and represents a major public health success in primary prevention efforts to eliminate lead hazards. The decline in blood lead levels is the topic of a companion article.[19]

The findings from NHANES III phase 1 demonstrate, however, that a substantial proportion of US children younger than 6 years (8.9%) have blood lead levels now considered a health concern (≥0.48 µmol/L [≥10 µg/dL]). These levels continue to vary markedly by age, sex, race/ethnicity, urban status, income, and other sociodemographic factors. Blood lead levels were consistently higher for younger children than for older children, for older adults than for younger adults, for males than for females, for blacks than for whites, and for central-city residents than for non–central-city residents. Other correlates of higher blood lead levels included low income, low educational attainment, and residence in the Northeast region of the United States. Prevalence estimates of elevated blood lead levels from recent studies based in clinics, private, and other health care practices are consistent with the current estimates for young children.[20-24]

The variability of the estimates in this article may reflect differences in the absorption, metabolism, and excretion of lead or in the degree of environmental lead exposure. Lead is more readily absorbed by young children than by adults, but variations in other metabolic processes (eg, mobilization of lead from bone during pregnancy or during the aging process) have not been widely investigated.[25] Deficiencies in nutritional status, particularly those resulting from low iron and calcium intake, may also affect lead absorption.[26]

The primary strength of NHANES III is its ability to provide standardized estimates of blood lead levels in the US population using a high degree of both protocol standardization and laboratory QC. With the completion of the second phase of the survey, the increase in sample size will allow for a finer stratification of the population and a more comprehensive analysis of risk factors associated with lead.

A potential limitation to the design of the survey was the inability to examine the seasonal effect on blood lead levels. For logistical reasons, the mobile examination centers were located in the Northeast and Midwest in the summer months and in the South and West in the winter months. A seasonal variation in blood lead levels has been demonstrated[27] and may account for the apparent regional variability (higher blood lead levels in the Northeast) in this study. The NHANES III was also not designed to measure specific sources of lead exposure. However, sociodemographic variables can serve as indicators of the potential for lead in an individual's environment. Factors such as low income and minority status may predispose an individual to living in deteriorating, older housing or in a residential area where there is lead-contaminated urban soil and dust. Disparities in environmental lead exposure as a result of race/ethnicity, income, or geographic location have been extensively examined and are well documented.[5,25]

The public health threat posed by lead exposure may in fact be greater than the low mean blood lead levels in the general population suggest. Young children are at a greater risk for elevated blood lead levels because of their increased oral activity and ability to absorb lead coupled with the rapid development of the central nervous system in the first years of life.[28] Blood lead levels as low as 0.48 µmol/L (10 µg/dL), previously thought to be safe, have been associated with developmental delays, deficits in intellectual performance and neurobehavioral functioning,[28,29] decreased stature,[30,31] and diminished hearing acuity.[32] To address these findings, the CDC developed a multitiered approach to manage blood lead levels that are equal to or exceed the intervention level of 0.48 µmol/L (10 µg/dL).[18] Based on the results of NHANES III phase 1, approximately 1.7 million children aged 1 to 5 years in the United States are estimated to have blood lead levels exceeding this threshold. Since the publication of the current guidelines (October 1991), additional epidemiologic follow-up studies have demonstrated an inverse relationship between early exposure to low levels of lead and cognitive ability in later years.[33-35]

Of the multiple sources of exposure, lead-based paint is the principal high-dose source of lead. Exposure occurs through the direct ingestion of flaking or chalking paint or through inhalation of dust and soil contaminated with paint. Although lead-based paint was banned

Table 4.—Percentage of Children Aged 1 to 5 Years at or Above Selected Blood Lead Levels by Age Category and Race/Ethnicity: United States, 1988 to 1991

		Blood Lead Levels, %				
	Age, y	≥1.21 µmol/L (≥25 µg/dL)	≥0.97 µmol/L (≥20 µg/dL)	≥0.72 µmol/L (≥15 µg/dL)	≥0.48 µmol/L (≥10 µg/dL)	≥0.24 µmol/L (≥5 µg/dL)
All*	1-5	0.5	1.1	2.7	8.9	33.2
Non-Hispanic white	1-2	0.4	0.8	2.1	8.5	34.2
	3-5	0.4	0.4	0.7	3.7	21.3
Non-Hispanic black	1-2	1.4	5.4	10.2	21.6	63.9
	3-5	0.8	2.9	6.0	20.0	54.5
Mexican American	1-2	1.0	1.9	2.9	10.1	41.4
	3-5	0.7	0.7	1.4	6.8	34.5

*All includes race/ethnicity groups not shown separately.

Table 5.—Percentage of Children Aged 1 to 5 Years With Blood Lead Levels 0.48 µmol/L (10 µg/dL) or Greater by Race/Ethnicity, Income Level, and Urban Status: United States, 1988 to 1991

	All, %*	Non-Hispanic White, %	Non-Hispanic Black, %	Mexican American, %
Income level†				
Low	16.3	9.8	28.4	8.8
Mid	5.4	4.8	8.9	5.6
High	4.0	4.3	5.8	0.0§
Urban status‡				
Central city, ≥1 million	21.0	6.1§	36.7	17.0
Central city, <1 million	16.4	8.1	22.5	9.5
Non–central city	5.8	5.2	11.2	7.0

*All includes race/ethnicity groups not shown separately.
†Income level was defined by poverty-income ratio (PIR) categorized as low (0<PIR<1.30), mid (1.30≤PIR<3.00), and high (PIR≥3.00). Persons with missing information on income are not included in the analysis of income level.
‡Persons with missing information on urban status are not included in the analysis of urban status.
§Estimate may be unstable due to small sample size.

Table 6.—Coefficients From Linear Regression Analysis of Log_{10} Blood Lead Levels (µmol/L and µg/dL) by Age Group: United States, 1988 to 1991*

	Age, y				
Covariates	1-5	6-11	12-19	20-49	≥50
Age, y	−.04 (.01)§	−.02 (.01)§	−.01 (.01)	.01 (0)§	0 (0)
Sex					
Male	.01 (.02)	.11 (.03)§	.34 (.04)§	.34 (.02)§	.16 (.01)§
Female†	0	0	0	0	0
Race/ethnicity					
Non-Hispanic black	.14 (.03)§	.18 (.04)§	.15 (.04)§	.09 (.03)§	.12 (.01)§
Mexican American	.09 (.03)§	.12 (.05)‖	.12 (.06)	.04 (.03)	−.01 (.04)
Non-Hispanic white†	0	0	0	0	0
Poverty-income ratio	−.04 (.01)§	−.07 (.01)§	−.03 (.01)	−.02 (.01)§	−.01 (0)‖
Education‡					
Less than high school	.13 (0.2)§	.11 (.03)§	.16 (.04)§	.12 (.03)§	.02 (.02)
At least high school†	0	0	0	0	0
Urban status					
Central city, ≥1 million	.17 (.03)§	.11 (.09)	.26 (.05)§	.07 (.03)‖	.06 (.02)‖
Central city, <1 million	.09 (.04)‖	.04 (.05)	.02 (.05)	.01 (.02)	.02 (.02)
Non–central city†	0	0	0	0	0
Region					
Midwest	−.14 (.04)§	−.14 (.07)	−.16 (.12)	−.11 (.04)‖	−.11 (.03)§
South	−.22 (.04)§	−.21 (.06)§	−.17 (.10)	−.19 (.03)§	−.18 (.03)§
West	−.32 (.05)§	−.33 (.09)§	−.20 (.12)	−.14 (.05)‖	−.15 (.03)§
Northeast†	0	0	0	0	0
R^2	.27	.28	.27	.31	.16

*SEs listed in parentheses.
†Last category serves as reference category for categorical variables.
‡The education of the adult reference person was used for those aged 1 to 19 years.
§$P<.01$.
‖$P<.05$.

in 1978, deteriorating lead-based paint in residential housing continues to present a significant challenge. In addition to paint, soil and dust also act as conduits for lead deposited from gasoline emissions and industrial sources. Lead found in drinking water as a result of lead solder and pipes used in water distribution systems also presents a source of exposure for children, and adults. Contaminated foods and cooking utensils as well as traditional ethnic medicines have been identified as other sources of lead exposure.[18,26]

Blood Lead Levels of Adults

Data from NHANES III phase 1 indicate that mean blood lead levels are low for young adults and higher for older adults. The distribution of elevated blood lead levels (≥0.48 µmol/L [≥10 µg/dL]) follows a similar pattern, although the proportions of levels 1.21 µmol/L (25 µg/dL) or greater were 0.5% or lower for every adult age group. The low prevalence of high blood lead levels is consistent with the fact that nonindustrial lead toxicity among adults is rare. Of adults with blood lead levels 1.21 µmol/L (25 µg/dL) or greater, it is estimated that 95% of these high levels are attributable to occupational exposure.[36] Nonetheless, occupational exposure to lead remains a concern, particularly for those who work in smelters, construction, demolition, and automobile repair.[37] The similar demographic correlates of blood lead levels across age groups suggest that sources of exposure associated with urbanization and poverty, such as deteriorated lead paint and urban dust, may be important factors for adults as well as children.

Beyond the workplace, there is an interest in understanding the potential neurotoxic effects of lead that may occur when lead is released from bone as part of the aging process.[38,39] In NHANES III phase 1, the highest geometric mean blood lead levels in adults were seen in males aged 70 years and older. If blood lead levels in the older population are more influenced by past exposure as a result of the mobilization of bone lead stores, one might expect that with recent reductions in lead exposure the levels of older persons would decrease less than the levels of younger persons. Nonetheless, the reasons for higher blood lead levels among older adults and their health significance are unclear. The low R^2 (.16) in the NHANES III phase 1 regression model for older adults underscores the need to examine risk factors that may help to explain the variation in blood lead levels

in this subpopulation. In view of studies suggesting that blood lead levels may be causally associated with higher blood pressure[40] and impaired renal function[41] in adults, further research is warranted on the relation between cumulative lead exposure and health problems associated with aging.

Blood Lead Levels of Women of Childbearing Age

The NHANES III phase 1 data indicate that mean blood lead levels for reproductive-aged females are low relative to the rest of the population. However, some data suggest an association between low blood lead levels (<0.48 µmol/L [<10 µg/dL]) measured from umbilical cord blood (which correlates well with maternal blood lead levels) and subsequent deficits in cognitive test performance and neuromotor performance in children.[28] In addition, lead from prior environmental exposure released from the bone during pregnancy may result in lead toxicity to both the mother and the fetus.[42] Unfortunately, the small number of NHANES III phase 1 women who were pregnant at the time of examination precludes a separate analysis of pregnant women and national estimates of fetal lead exposure.

CONCLUSIONS

Blood lead estimates from NHANES III phase 1 offer evidence supportive of the major achievements made in controlling lead exposure during the past decades. However, current knowledge of the health effects of low-level lead exposure underscores the benefits of past reductions at the same time as it makes clear the impact of the remaining lead exposure problem. Disproportionately, children who are minorities, poor, and living in urban areas may be at a significant risk for exposure to harmful levels of lead. Disparity in exposure to environmental hazards such as lead contributes to differences in morbidity and mortality among subgroups of the population defined by these important sociodemographic factors.[43] A concerted effort to identify the vulnerable risk groups will be vital to further reductions in lead exposure.

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Appendix A.2

COSTS AND BENEFITS OF A UNIVERSAL SCREENING PROGRAM FOR ELEVATED BLOOD LEAD LEVELS IN 1-YEAR-OLD-CHILDREN

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Abstract

Background. In 1991, the Centers for Disease Control recommended screening all children for elevated blood lead levels, that is blood lead levels of at least 10 micrograms per deciliter, except in communities where large numbers or percentages of children have been screened and found not to have lead poisoning. We have quantitatively compared the economic costs and benefits of universal screening to help refine guidance on screening and to define information gaps in evaluating the effectiveness, cost-effectiveness, and economic benefits of blood lead screening.

Methods. We used mathematical simulations of a blood lead level screening program to estimate the costs and benefits of universal screening as the prevalence of elevated blood lead levels varied. To do this, we estimated 1) the distribution of elevated blood lead levels in 1-year-old children, 2) the accuracy of blood lead screening tests, 3) the costs of screening for and intervening to reduce elevated blood lead levels, 4) the effectiveness of interventions to reduce blood lead levels, 5) the relationship of elevated blood lead levels to adverse health outcomes, and 6) the economic costs of lead-related adverse health effects.

Results. As the observed prevalence of elevated blood lead levels increased, the cost, effectiveness, and economic benefits of universal screening increased. When more than 14% of children had elevated blood lead levels, the economic benefits of universal screening exceeded the costs. When less than 14% of children had elevated blood lead levels, the costs of universal screening exceeded the benefits. The simulations were reasonably robust to changes in most assumptions; changing most assumptions within broad ranges resulted in relatively modest changes in the threshold prevalence at which benefits of screening exceeded the costs within a range of 11% to 17%. This threshold prevalence was, however, very sensitive to the estimated effectiveness of educating families of children with elevated blood lead levels about ways to reduce lead exposures and, to a lesser extent, to the estimated costs and effectiveness of environmental interventions for reducing children's blood lead levels.

Discussion. In mathematical simulations of a blood lead screening program, universal screening for elevated blood lead levels produced economic benefits exceeding program costs in communities where at least 11% to 17% of children had elevated blood lead levels. In communities with lower prevalences of elevated blood lead levels, universal screening may be inefficient or ineffective in improving children's health and development; in lower prevalence communities, other strategies such as more targeted screening, reducing lead exposure sources in the environment, and educating families about lead hazards and ways to avoid them may be preferable to testing every young child for an elevated blood lead level. Additional studies to better evaluate the effectiveness and cost-effectiveness of interventions to reduce children's blood lead levels, especially relatively low blood lead levels, are needed.

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Appendix A.3

RELATIONSHIP BETWEEN PREVALENCE OF BLLS ≥10 μg/dL AND PREVALENCES ABOVE OTHER CUT-OFF LEVELS

Prevalences of elevated BLLs represent distributions of BLLs in children and are a shorthand for these BLL distributions. BLLs in populations usually are log-normally distributed. That is, in any population, BLLs are distributed normally on a log-scale and are skewed toward lower BLLs on the arithmetic scale.

On the basis of these distributions, if the prevalence of BLLs that are 10 μg/dL or greater is known, it is possible to estimate the prevalences of elevated BLLs at other cut-off points. For example, the prevalence of BLLs 15 μg/dL or greater (the threshold for environmental intervention for individual children) or BLLs 20 μg/dL or greater (the threshold for medical management) can be estimated.

To arrive at these estimates, some assumptions about the variability of BLLs in the population must be made. One measure of such variability is the geometric standard deviation (GSD). For this document, we estimated that a GSD of 1.9 reflects typical variability in lead exposure in many communities in the United States. We selected it to be higher than the range of 1.67-1.79 reported in several recent studies of children living near lead smelters.[1]

Children living near smelters are likely to have less variability in BLLs than is typical since all children in those communities share a single large source of lead exposure. In contrast, we selected a value that was less than the 2.12 recently measured in a probability sample of U.S. children in NHANES III [1] because the national estimate includes variability among communities that is not relevant in any single place.

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[1] The underlying population distribution is assumed to be log-normal with a geometric standard deviation (GSD) of 1.9. If lead exposure is extremely heterogeneous, this GSD will be an underestimate and, at any given geometric mean, the proportion of children with very high BLLs may be greater. If lead exposure is unusually homogenous, this GSD may be an overestimate and, at any given geometric mean, the proportion of children with very high BLLs may be lower.

Appendix A.4

EXACT CONFIDENCE INTERVALS FOR SOME HYPOTHETICAL ESTIMATES OF PREVALENCE OF BLLs ≥ 10 µg/dL, BY NUMBER OF CHILDREN SCREENED.[1]

Estimated prevalence sample	Number screened	95% confidence intervals[2] in lower	upper
1%	100	< 1%	5%
	200	< 1%	4%
	400	< 1%	3%
	1000	< 1%	2%
2%	50	< 1%	11%
	100	< 1%	7%
	200	1%	5%
	400	1%	4%
	1000	1%	3%
3%	100	< 1%	9%
	200	1%	6%
	400	2%	5%
	1000	2%	4%
4%	50	< 1%	14%
	100	1%	10%
	200	2%	8%
	400	2%	6%
	1000	3%	5%
6%	50	1%	17%
	100	1%	13%
	200	3%	10%
	400	4%	9%
	1000	5%	8%
8%	50	2%	19%
	100	4%	15%
	200	5%	13%
	400	5%	11%
	1000	6%	10%
10%	50	3%	22%
	100	5%	18%
	200	6%	15%
	400	7%	13%
	1000	8%	12%
11%	100	6%	19%
	200	7%	16%
	400	8%	14%
	1000	9%	13%
12%	50	5%	24%
	100	6%	20%
	200	8%	17%

Appendix A.5

OCCUPATIONAL AND HOBBY SOURCES OF LEAD POISONING

Occupational sources of lead poisoning for adults

- Secondary smelting and refining of nonferrous metals
- Storage batteries (lead batteries)
- Valve and pipe fittings (except plumber's brass goods)
- Plumbing fixture fittings and trim (brass goods)
- Brass or copper foundries
- Glass products made of purchased glass
- Motor vehicle parts and accessories
- Firing ranges
- Pottery
- Chemical and chemical preparations
- Bridge, tunnel, and elevated highway construction
- Automotive repair shops
- Industrial machinery and equipment
- Inorganic pigments
- Primary batteries, dry and wet

Hobby sources of lead poisoning

- Using firing ranges
- Making home repairs or remodeling homes
- Refinishing furniture
- Making stained glass
- Casting ammunition
- Making fishing weights or toy soldiers
- Using lead solder (for example, for electronics)
- Using artists' paints that contain lead
- Burning wood painted with lead-based paint
- Repairing cars or boats
- Making fishing sinkers

Adapted from the 1991 edition of *Preventing Lead Poisoning in Young Children* and ATSDR *Case Studies in Environmental Medicine: Lead Toxicity*.

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Appendix B.1

THE LEAD LABORATORY

Patrick J. Parsons, Ph.D.[1]

Role of the Laboratory

Laboratories measure lead concentrations in either clinical samples such as blood and urine or in environmental samples such as paint and dust. It is important to distinguish between the clinical and environmental lead laboratories and the issues that they face. Often, laboratories are separated according to the types of samples they analyze even though the technologies used to measure lead levels may be similar.

Several reasons exist for separating laboratories along sample lines. For example, clinical and environmental laboratories operate under different federal or state regulations. Sample handling and reporting requirements of state and federal agencies differ, as do requirements for quality control. The reportable concentration range for lead in blood is quite different from that for lead in paint or in dust, and the preparation of the sample requires different procedures.

Further, the higher concentrations of lead typically found in lead-based paint (> 0.5% by weight) and in lead-contaminated dust (> 1 mg/g) present the potential for contaminating the laboratory environment. If environmental and clinical laboratory functions are carried out in the same laboratory room, determination of the much lower concentrations of lead found in blood is jeopardized.

For all *clinical* laboratories in the United States, the Health Care Financing Agency (HCFA), operating under the Clinical Laboratory Improvement Amendments of 1988, regulates all aspects of laboratory operation including determining the qualifications of a laboratory director and establishing protocols for quality assurance and quality control (QA/QC) activities, method validation, specimen collection, storage, analysis and reporting of results (42 CFR Part 493). For blood lead laboratories specifically, successful participation in an approved proficiency testing (PT) program is required. In addition, many states regulate the operation of clinical laboratories under their jurisdiction although the requirements vary greatly from state to state. Laboratories are advised to contact their state health department to ensure compliance with state and local laws.

For *environmental* laboratories, the primary regulatory agencies are the U.S. Environmental Protection Agency (EPA) and the National Institute for Occupational Safety and Health (NIOSH). In many laboratories, the EPA's Contract Laboratory Program (CLP) requirements drive all QA/QC activities and restrict the analytical protocol used. Several states also regulate environmental laboratories under their jurisdiction, although regulations vary from state to state.

The clinical lead laboratory

Determining lead levels in blood
A blood lead test is recommended for initial screening purposes, and for diagnostic evaluation. Serial blood lead measurements are recommended for monitoring patients under medical management.

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[1]*Wadsworth Center for Laboratories and Research, New York State Department of Health. Dr Parsons is also a consultant to CDC's Advisory Committee on Childhood Lead Poisoning Prevention.*

Appendix B.2

CAPILLARY BLOOD SAMPLING PROTOCOL

The high potential for lead contamination of specimens during collection is well known,[1-3] and some have suggested special steps to minimize the likelihood of contamination. These include thorough scrubbing of the hand and finger with soap and then alcohol,[4-5] using dilute nitric acid [6-7] or using silicone or a similar barrier spray.[3, 8-10] In three recent CDC-funded studies, results showed that using a silicone barrier spray did not reduce contamination errors in capillary blood collection protocols.[11-13] However, results of these studies also showed that capillary blood collection by fingerstick had very low (<10%) contamination error rates.

Various types of plastic microcollection containers (150 - 250 µL) are currently available and being used successfully to collect capillary blood from young children. Plastic containers are better than glass microhematocrit tubes, because the latter have been known to break, causing injury to laboratory personnel. The following procedure for collecting capillary blood specimens by fingerstick is recommended.

A. Materials Needed

- Soap
- Alcohol swabs. If a surgical or other disinfectant soap is used, alcohol swabs can be eliminated.
- Sterile cotton balls or gauze pads
- Examination gloves
- Lancets. The type of lanced used is largeley a matter of personal preference as long as sterility is guaranteed.
- Microcollection containers. The laboratory should be consulted beforehand about the type of device it will accept. Some laboratories will provide "lead-free" tubes for blood lead screening purposes.
- Adhesive bandages.
- Trash bags suitable for medical waste and containers for sharps. Bags containing medical waste should be clearly identified as such.
- Storage or mailing containers if needed. If specimens require shipment, follow the U.S. P.S. or other appropriate regulations for the transport of body fluids.
- Laboratory coat and protective glasses.

Materials used in the collection procedure that could contaminate the specimen (for example, blood containers, alcohol swabs, and barrier sprays) must be lead-free. **Before selecting equipment for use in blood collection, consult the laboratory about its requirements.** In many cases, the laboratory will recommend or supply suitable collection equipment and may precheck the equipment for lead contamination. Some instrument manufacturers also supply collection materials that are pretested for lead content.

B. Preparing for Blood Collection

All personnel who collect specimens should be well trained in and thoroughly familiar with the collection procedure and the use of universal precautions against the transmission of blood-borne pathogens. The skill of the collector will greatly influence the specimen quality. All

Appendix B.3

Table A.
PROFICIENCY TESTING PROGRAMS FOR LEAD LABORATORIES

Agency	Analytes	Licencing/Certification	Program contact
Health Resources and Services Administration (HRSA) Wisconsin State Laboratory of Hygiene (WSLH) Telephone: (608) 262-1146	Blood lead, EP	OSHA,HCFA (some states)	Noel Stanton Wisconsin State Laboratory of Hygiene Madison, WI 53706
College of American Pathologists (CAP) American Association for Clinical Chemistry (AACC) Telephone: (800) 323-4040	Blood lead, EP	OSHA,HCFA (some states)	Survey Coordinator 325 Waukegan Road Northfield, IL 60093
New York State Department of Health (NYSDOH) Telephone: (518) 474-8739	Blood lead, EP	OSHA,HCFA (State of New York)	Dr. Patrick Parsons Wadsworth Center Laboratories NYS DOH, PO Box 509 Albany, NY 12201-0509
Pennsylvania Department of Health (PADOH) Telephone: (215) 363-8500	Blood lead, EP	OSHA,HCFA (State of PA)	Dr. M. Jeffrey Shoemaker PA DOH Bureau of Laboratories Pickering Way & Welsh Rd Lionville, PA 19353
Puerto Rico Department of Health (PR DOH) Telephone: (809) 764-6945	Blood lead	HCFA	Lab. Services Program Department of Health Building A Call Box 70184 San Juan, PR 00936
Centre de Toxicologie du Quebéc (CHUL) Telephone: (418) 654-2100	Blood lead	none	Dr. Jean-Phillipe Weber Lab. de Toxicologie CHUL 2705 Boul. Laurier, Sainte-Foy, Quebéc CANADA G1V 4G2
Environmental Lead Proficiency Analytical Testing (ELPAT) American Industrial Hygiene Association (AIHA) National Institute for Occupation Safety & Health (NIOSH) Centers for Disease Control and Prevention (CDC) Environmental Protection Agency (EPA) Telephone: (703) 849-8888	Paint lead Soil lead Dust lead	National Laboratory Accreditation Program	ELPAT Coordinator AIHA, 2700 Prosperity Ave. Fairfax, VA 22031

Appendix B.3

Table B.
QUALITY CONTROL MATERIALS FOR USE IN BLOOD LEAD TESTING

Source	Product	Description	Certified lead levels
Bio-Rad, ECS Division 1000 Alfred Nobel Drive, Hercules, CA 94547 Telephone: (800)227-1600	Lyphocheck®	Whole blood control (human)	3
Centers for Disease Control and Prevention (CDC) Blood Lead Laboratory Reference System (BLLRS) Mailstop F18, 4770 Buford Highway NE Atlanta, GA 30341-3724 (404) 488-	BLLRS bovine blood	Reference Materials for blood lead (target values established by IDMS, using ICP-MS)	5-8
Ciba-Corning Diagnostics Corporation 63 North Street, Medfield, MA 02052 (800) 255-3232	BLD TOX I, II	Whole Blood Toxicology Control	2
Commission of the European Communities (CEC) Community Bureau of Reference (BCR) Rue de la Loi 200, B-1049, Brussels, Belgium 32 2 2955014	BCR No 194-196	Lead and Cadmium in Blood (target values established by reference labs	3
Kaulson Laboratories, Inc. 687-691 Bloomfield Ave., West Caldwell, NJ 07006 (201) 226-9494	Contox®	Control materials for blood lead	6
National Institute of Standards and Technology (NIST) Office of Standard Reference Materials - Room 205 Gaithersburg, MD 20899 Telephone: (301) 975-6776	SRM 955a	Freeze-dried blood reference materialsfor blood lead (target values established by reference labs)	4

Table B. (continued)
QUALITY CONTROL MATERIALS FOR USE IN BLOOD LEAD TESTING

Source	Product	Description	Certified lead levels
New York State Department of Health (NYSDOH) Wadsworth Center Labs. Rm D146 PO Box 509 Albany, NY 12201-0509 (518) 473-0452	NYS-RM	Freeze-dried blood reference materials for blood lead	3
Nycomed Pharma AS Accurate Chemical and Scientific Corp., 300 Shames Drive, Westbury, NY 11590)	Seronorm™	Trace elements whole blood	3
Utak Laboratories, Inc. 26752 Oak Ave., Canyon Country, CA 91351	Whole blood lead control	Lyophilized human blood	3 or 4

Appendix B.3

Table C.
QUALITY CONTROL MATERIALS FOR USE IN URINE LEAD TESTING

Source	Product	Description	Certified lead levels
Bio-Rad, ECS Division 1000 Alfred Nobel Drive, Hercules, CA 94547 Telephone: (800)227-1600	Lyphocheck® Lyphocheck®	Urine metals control Quantitative urine controls	2 2
Ciba-Corning Diagnostics Corporation 63 North Street, Medfield, MA 02052 (800) 255-3232	URINE I, II	Control urine	2
Fisher Scientific Address Orangeburg, NY 10962	Uri Chem®	Urine chemistry control	2
Kaulson Laboratories, Inc. 687-691 Bloomfield Ave., West Caldwell, NJ 07006 (201) 226-9494	Contox®	QC materials for urine lead testing	3
National Institute of Standards and Technology (NIST) Office of Standard Reference Materials - Room 205 Gaithersburg, MD 20899 Telephone: (301) 975-6776	SRM 2670	Toxic metals in freeze-dried urine	6
New York State Department of Health (NYSDOH) Wadsworth Center Labs. Rm D146 PO Box 509 Albany, NY 12201-0509 (518) 473-0452	Freeze-dried urine	Reference materials for urine lead testing	2
Nycomed Pharma AS Accurate Chemical and Scientific Corp., 300 Shames Drive, Westbury, NY 11590	Seronorm™	Trace elements urine	3
Utak Laboratories, Inc. 26752 Oak Ave., Canyon Country, CA 91351	Urine metals control	Lyophilized human urine	2

Appendix B.3

Table D.
QUALITY CONTROL MATERIALS FOR ERYTHROCYTE PROTOPORPHYRIN TESTS

Source	Product	Description	Certified lead levels
Aviv Biomedical Inc P.O. Box 994 750 Vassar Avenue Lakewood, NJ 07006 Telephone: (908) 370-1300	Red blood cell controls	BLood-based controls for the hematoflourometer	3
Kaulson Laboratories, Inc. 687-691 Bloomfield Ave., West Caldwell, NJ 07006 Telephone: (201) 226-9494	Contox®	QC materials for EPP, ZPP	4
Helena Laboratories 1530 Lindbergh Drive Beaumont, TX 77704 Telephone: (800) 231-5663	Protofluor™	Calibrators for the PF-Z	2
New York State Department of Health (NYSDOH) Wadsworth Center Labs. Rm D146 PO Box 509 Albany, NY 12201-0509 Telephone: (518) 473-0452	EP Controls	Freeze-dried whole blood for EP	3
Wadsorth Center Laboratiers Room D146 P.O. Box 509 Albany, NY 12201-0509 Telephone: (518) 473-0452	ZPP Materials	Blood-based controls for the Hematoflurometer	5

equipment should be within easy reach. The environment should be clean, secure, and as nonthreatening to the child as possible. Any necessary consent should be obtained before specimen collection begins, and the procedure should be explained to the child and the parent or guardian. Used materials should be immediately discarded into appropriate medical waste containers

C. Preparing the Finger for Puncture

NOTE: Puncturing the fingers of infants younger than 1 year of age is not recommended. Puncturing of the heel or toe may be more suitable for these children.[14]

Collection personnel should wear examination gloves whenever the potential for contact with blood exists. If the gloves are coated with powder, the powder should be rinsed off with tap water.

The child's hands should be thoroughly washed with soap and then dried with a clean, low-lint towel. Plain, unprinted, nonrecycled towels are best.[15] If desired, collection personnel can use a brush to clean the finger; brushing the finger during washing can increase blood circulation in the finger.[9] Once washed, the clean finger must not be allowed to come into contact with any surface, including the child's other fingers.

The finger to be punctured (often the middle finger) must be free of any visible infection or wound; it should be massaged to increase circulation before being punctured with the lancet. This massage can be done during or after washing.[9, 10]

Steps for Preparing the Child's Finger

1. Select examination gloves. If necessary, rinse them to remove powder.

2. Wash the child's hands thoroughly with soap and water, and then dry them with an appropriate towel.

3. Grasp the finger that has been selected for puncture between your thumb and index finger with the palm of the child's hand facing up.

4. If not done during washing (see preceding notes), massage the fleshy portion of the finger gently.

5. Clean the ball or pad of the finger to be punctured with the alcohol swab. Dry the fingertip using the sterile gauze or cotton ball.

Puncturing the Finger

After the finger is prepared, the puncture and subsequent steps of forming a drop of blood and filling the collection container should be performed quickly and efficiently, since any delay can make collection more difficult (for example, the blood may clot or the child may resist). Several types of lancets are suitable for puncturing children's fingers. Lancets range from small manual blades and spring-loaded assemblies to disposable self-contained units. The latter are particularly attractive since the blade is automatically retracted into the holder after use, thus reducing the risk for self injury. Many devices are available with a selection of puncture depths suitable for small children or adults. Regardless of the type of lancet used, make the puncture swiftly, cleanly, and deep enough to allow for adequate blood flow.

The site of the puncture should be slightly lateral to the ball of the finger. This region is generally less calloused, which makes puncturing easier and possibly less painful.[9] The first drop of blood contains tissue fluids that will produce inaccurate results; it should be removed with a sterile gauze or cotton ball.[9,10]

A barrier material, such as silicone that is sprayed on the finger at this point in the process, will help a distinct "bead" of blood to form and may aid in blood collection. Blood that runs down the finger or around the fingernail is no longer suitable. Blood flows better when the punctured finger is kept lower than the level of the heart. Inadequate blood flow can be improved by gently massaging the proximal portion of the finger in a distal direction, then pressing firmly at the distal joint of the punctured finger (restricting blood flow out of the fingertip) and gently squeezing the sides of the fingertip. Avoid excessive squeezing or milking" which will cause tissue fluid to be expressed, compromising specimen integrity.[9,10]

Steps for Puncturing the Finger and Forming Drops of Blood

1. Grasp the finger and quickly puncture it with a sterile lancet in a position slightly lateral to the center of the fingertip.

2. Wipe off the first droplet of blood with a sterile gauze or cotton ball.

3. If blood flow is inadequate, gently message the proximal portion of the finger and then press firmly on the distal joint of the finger.

4. A well-beaded drop of blood should form at the puncture site.

5. Do not let the blood run down the finger or onto the fingernail.

E. Filling the Collection Container

The proper procedure for filling and capping collection containers is somewhat specific to the container used. As a general rule, contact between the skin and the container should be avoided. To prevent specimen clotting, blood must be thoroughly mixed with the anticoagulant after filling the container. Depending on the container and anticoagulant used, the agitation needed can range from gentle rocking to vigorous shaking. Some procedures call for the collection container to be rotated during filling so that anticoagulant will be distributed quickly through the sample.[16] For collectors already familiar with fingerstick blood collection for other purposes (e.g., hematocrit or CBC), there is a tendency to not agitate the blood sample too strongly lest the red blood cells rupture. For blood lead tests vigorous agitation is not an issue because it is more important to prevent clotting than cell rupture.

To facilitate blood flow, many procedures call for the collection container to be held nearly horizontal, with a slight downward angle. Blood flow into the container should be uninterrupted to avoid getting air bubbles in the specimen. Most containers come with appropriate caps, and these should be applied immediately after collection. Again, consulting with the laboratory and knowing the manufacturer's recommendations are important to ensure specimen integrity and suitability for analysis.

Steps For Filling The Collection Container

1. Continuing to grasp the finger, touch the tip of the collection container to the beaded drop of blood.

2. Draw the blood into the container maintaining a continuous flow of blood.

3. When the container is full, cap or seal it as appropriate.

4. Agitate the specimen to mix the anticoagulant through the blood.

5. Check that the container is properly labeled, and place it in an appropriate storage area.

6. Stop the bleeding, and cover the finger with an adhesive bandage. Bleeding should stop quickly. If bleeding is slow to stop, apply pressure to the puncture site with a sterile gauze or a cotton ball. If bleeding continues after 3 to 5 minutes of applying pressure, consult a physician.

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Specimen collection
Capillary blood lead measurements may be used for initial screening purposes, but only venous blood is appropriate for diagnostic evaluation, and a venous BLL is necessary before initiating an environmental investigation or chelation therapy. From 1991 to 1994, CDC sponsored several studies to evaluate the performance of capillary blood lead screening by comparing blood lead levels in specimens obtained by fingerstick with those obtained simultaneously by venipuncture.

Results of studies conducted by Yale New Haven Hospital and the Connecticut Department of Health, the City of Milwaukee, and the New York State Department of Health, independently concluded that, *provided that a strict cleaning protocol is followed*, capillary whole blood obtained by fingerstick is a reliable specimen for pediatric lead screening purposes.

Most capillary blood specimens that show falsely elevated lead levels can be traced to inappropriate collection procedures or to contaminated materials used to collect and transport the specimen.[1] For these reasons, laboratories should ensure that all materials used to collect capillary blood specimens are free from significant lead contamination. It is recommended that capillary blood be collected in plastic microcollection devices containing either EDTA (lavender caps) in powder form or heparin (green caps) rather than glass capillary tubes, which can break and may result in injury and disease transmission.

The choice of microcollection container is a matter for each individual laboratory and depends on factors such as the desired sample volume or anticoagulant type. Although capillary blood is useful for initial screening, only venous blood should be used for diagnostic evaluation or medical management. A recommended procedure for collecting capillary blood by fingerstick is given in Appendix B.2.

Recommended procedures for controlling contamination

Perhaps the most frequent source of error is contamination by airborne particulates containing lead. Although use of lead in gasoline and paint has been reduced, lead still remains a ubiquitous pollutant, especially in common dust. Therefore, special precautions must be taken to prevent contamination during specimen collection and analysis. These precautions include checking all collection materials and supplies for significant contamination and using dust-control measures in the laboratory as recommended below.

Some manufacturers provide blood collection tubes specifically for trace element analysis (royal blue caps) or certified lead-free tubes for blood lead level determination (tan/brown caps). Laboratories should check lead-free claims made by individual manufacturers before using such devices since the amount of lead in these devices is reported to vary greatly.

Once a reliable source of certified lead-free materials has been located, laboratories need not check each individual lot for lead contamination. Since the cost of certified lead-free tubes is likely to be much more than for standard tubes, some laboratories may prefer to obtain the standard tubes and certify them as lead-free for their clients as described below. This strategy will hold down the costs associated with BLL screening.

Checking collection materials and supplies
Two approaches may be used to assess contamination and ensure that materials are not significantly contaminated with lead. First select at least 10 collection devices at random from a

batch to test. The take either of these two steps:

- Fill specimen or sample containers with either dilute acetic acid (4% v/v) or dilute nitric acid (2% v/v) and store for 24 hours at room temperature. Analyze leachate for lead and calculate the total amount of lead extracted.

- Fill specimen or sample container with a base low-lead blood sample of known lead concentration, and store for a period and under conditions the laboratory maintains for routine patient samples. Analyze the blood for lead levels to ascertain whether or not any significant lead contamination has occurred.

For both methods, any measurable increase in lead concentration should amount to no more than 0.5 μg/dL (i.e., 5% at 10 μg/dL). Needles, lancets, and materials other than containers should also be checked for gross contamination by leaching with a minimum volume of dilute acetic or dilute nitric acid and analyzing the leachate for lead. Generally, such materials should be free of significant contamination (i.e. < 1 μg/L or roughly the detection limit by graphite furnace atomic absorption spectrometry [GFAAS]).

In the laboratory, the handling of all blood is governed by the Occupational Safety and Health Administration's (OSHA's) blood borne pathogens rule (29 CFR Part 1910.1030), which specifies that CDC Universal Precautions must be used. For example, blood dilutions may be performed in a Class II biosafety cabinet using powder-free protective gloves. This procedure will not only protect the analyst from pathogens but will also protect the sample from airborne lead contamination.

Most clinical laboratories are not equipped with Class 100 air or better, nor do they need to be, as long as some basic consideration is given to the potential for airborne contamination at the bench. Autosampler vials should be screened for lead contamination until a lead-free supply is verified and should be stored protected from dust (e.g., in sealed plastic bags). Autosampler vials that are in use should be protected with appropriate dust covers. Frequent wet-mopping of laboratory floors and wet-wiping of other flat surfaces will minimize contamination from airborne dust particulates.

Transporting or shipping blood specimens to centralized laboratories

Currently, most blood lead testing is performed by a centralized laboratory that is licensed for this purpose. Consideration needs to be given to the most cost-effective and reliable way to transport specimens to the laboratory. Although some laboratories may use a network of couriers to transport specimens to the laboratory, others rely on the United States Postal Service (USPS) or commercial carriers to deliver specimens. Transport of etiologic agents (e.g., human blood) via USPS is regulated (42 CFR Part 72), and many commercial carriers may have similar restrictions.

Federal regulations require that blood specimens be packaged according to guidelines requiring the use of tertiary containment and sufficient absorbent material in the event that the specimen leaks during transit. When mailing glass tubes containing blood, ensuring that the tubes cannot touch during transit may reduce chances of breakage.

Venous blood specimens preserved with EDTA or heparin are reportedly stable for determining lead levels in blood for up to 10 weeks if they are refrigerated at 4°C.[2] Refrigerated temperatures are not necessary for mailing blood lead specimens. However, where significant delays are expected, as might occur over a holiday weekend, it would be prudent to store the samples locally, refrigerated at 4 °C, and

then ship them the next business day. In special circumstances, such as *stat* requests, blood specimens should be mailed overnight and the laboratory forewarned to expect them.

Analytical Methods For Determining Blood Lead Levels

Several analytical methods have been applied successfully to the determination of lead in blood. The methods most commonly in use today are either GFAAS or anodic stripping voltammetry (ASV). Other analytical methods include variations on AAS, such as methylisobutylketone (MIBK)-extraction flame AAS,[3] Delves-cup microsampling flame AAS,[4] and an inductively-coupled plasma interfaced to a quadrupole mass spectrometer (ICP-MS).

Beginning in 1992, CDC funded several innovative research projects aimed at developing portable instrumentation for determining lead levels in blood. Techniques under investigation include attempts to miniaturize AAS and atomic emission spectrometry (AES) and to develop various electrochemical approaches and polymeric sensors. Although each of these techniques has advantages and disadvantages, and although the new technologies may result in commercially available instruments in the future, we review only GFAAS and ASV in detail here.

Graphite Furnace Atomic Absorption Spectrometry

GFAAS has been successfully used to determine lead levels in blood.[5-8] Modern furnace instrumentation is reliable, accurate and precise and can be reasonably automated. Several manufacturers currently market GFAAS instruments that are readily configured for blood lead testing. Most of these instruments are also capable of measuring many more elements.

Selecting suitable GFAAS instruments should be done only after a careful evaluation of available commercial instruments. Prospective users should request that the manufacturer provide references from customers currently performing blood lead determinations and provide evidence of successful participation in an approved PT program for measuring blood lead levels. Numerous instrumental configurations and features are available.

Most commonly employed instruments use either the Zeeman-effect or continuum background correction systems, and some have successfully used the Smith-Heifjte background correction system. Each system can correct for nonspecific background at 283.3 nm, the principal analytical wavelength for lead.

Using the Zeeman-effect background correction system is more straightforward than using a continuum source; although the latter is less expensive, it can be difficult to optimize since two radiation sources (hollow cathode and continuum) are used, both of which must be carefully aligned along the optical path of the graphite furnace.

Many GFAAS methods for measuring blood lead levels using a variety of furnace instruments[9] have been published.* Until recently, it was thought that no one method for determining blood lead levels could be recommended for all instrumentation because of the complexity and differences between furnace equipment from the various manufacturers. However, recent experience has shown that a common or standard method for determining blood lead by GFAAS is possible.[8] This

**A selected list of methods of measuring blood lead levels and obtaining information about instrument manufacturers and other information pertinent to the clinical laboratory is available from CDC's National Center for Environmental Health, Division of Environmental Health Laboratory Sciences, Nutritional Chemistry Branch, MS F 18, 4770 Buford Highway, N.E., Atlanta, Georgia 30341-3274, telephone (770) 488-4452.*

method, which uses longitudinal Zeeman background correction and a transversely-heated furnace draws upon the work of both Pruszkowska et al.,[5]and Miller et al.[7] This simple, but rapid Zeeman AAS method for measuring blood lead levels has been successfully transferred to a simpler furnace arrangement that uses continuum background correction [10] and to other furnace AAS equipment using transverse Zeeman, continuum, and Smith-Heifjte background correction systems. [11,12]

Such standard methods are successful because they follow the stabilized temperature platform furnace (STPF) concept.[13] For a detailed description of the STPF approach to GFAAS method development, consult the appropriate references.[13,14] One critical component of the STPF approach is use of a suitable matrix modifier, which is required to stabilize lead during pyrolysis at temperatures exceeding 600°C and which will increase the volatility of the interfering matrix. Ammonium phosphate, either in the monobasic, $NH_4H_2PO_4$, or dibasic form of ammonium phosphate, $(NH_4)_2HPO_4$, along with Triton X-100 is now the most widely used modifier for determining blood lead levels by GFAAS.

Another important aspect of the STPF approach calls for using the L'vov platform for atomization coupled with integrated peak areas for absorbance measurements. Optimizing lead atomization from the platform rather than from the wall reduces gas-phase interferences and permits calibration against aqueous lead standards. Precision is also much improved over peak height measurements.

Most modern GFAAS instruments are equipped with autosamplers, which are useful for large numbers of samples and provide for unattended operation with better precision. The number of replicate firings that should occur depends on the method within-run precision, which should be less than ± 0.5 μg/dL at 10 μg/dL (5%). Replicate firings are recommended if the within-run precision is greater than 10%. When using the Delves-cup microsampling flame AAS method, where the within-run precision at 10 μg/dL can be as much as 40% (± 4 μg/dL), carry out the analysis in triplicate. Note that this precision is different from the concept of analytical accuracy, for which federal and some state authorities require results of performance samples to be accurate to within ± 4 μg/dL (or ± 10%, whichever is greater) of the established target value.

Other spectrometric techniques have been used to determine blood lead levels with varying degrees of success. Inductively coupled plasma-mass spectrometry (ICP-MS) is a powerful technique that not only can detect very low concentrations of lead but can also identify and quantify the lead isotopes present. The use of ICP-MS to determine blood lead levels includes limited attempts at source identification through isotope ratio fingerprints.[15] Unfortunately, this technique is currently an expensive solution that is not cost effective for routine blood lead measurements and is limited to a handful of specialized research laboratories.

Flame AAS, with chelation of lead and its extraction into MIBK solvent, is an older technique that requires a relatively large volume (5-7 mL) of venous blood for analysis.[3] Delves-cup microsampling flame AAS was developed specifically for determining blood lead levels in small blood volumes,[4] but, since the equipment and supplies are no longer available from AAS instrument manufacturers, it has been largely replaced by GFAAS.

Anodic stripping voltammetry (ASV)

Anodic stripping voltammetry (ASV) is a manual electrochemical method capable of measuring many metals in a variety of matrices. ASV has been used to determine blood lead

levels for more than 25 years. Several versions of instruments that are capable of performing this type of analysis are commercially available. The ASV technique is straightforward, and the instrumentation is relatively inexpensive, but reagent cost per test is higher than for GFAAS. ASV instruments are small, occupying less bench space than GFAAS, and require no special facilities. (GFAAS generally requires a 220 VAC, 30 A power supply.)

The analytical principle requires that lead be decomplexed and available for plating as the free +2 aqueous cation (Pb^{2+}_{aq}). One approach is to digest (wet ash) blood specimens with nitric acid, a time-consuming and laborious preanalytical step. More commonly, blood specimens are incubated in a solution containing several other metal ions that compete with lead for typical binding sites (proteins, amino acids, EDTA, and other biological ligands), and thus displace lead as the "free" cation.

One ASV instrument manufacturer provides a proprietary "decomplexation" solution along with two "controls" (or, more appropriately, calibrators) specifically for blood lead analysis. To perform a typical ASV analysis, a laboratorian uses a pipette to place 100 μL of anticoagulated whole blood into a tube containing a premeasured volume (2.9 mL) of the decomplexing reagent. The tube is placed in contact with the instrument electrode, and the analytical cycle is started. The concentration of lead in the blood is available in units of μg/dL within 90 seconds.

During the first 60 seconds of the 90-second analysis time, a negative potential is applied to a mercury-coated graphite electrode. (Other electrode designs have also been used.) This process results in the lead (as Pb^{2+}) "plating-out" (or dissolving) into the mercury coat. Usually, the potential is automatically and linearly swept back in a positive anodic direction. Other manufacturers may recommend functions other than a linear sweep (e.g., a square wave ASV). At a specific and characteristic voltage the lead is "stripped" from the electrode, a process that produces currents, the sum of which are proportional to the concentration of lead in the original sample. The samples may be prepared singularly or in a batch, and the analytical cycle is repeated for each sample. The operating parameters for analysis are normally established by the manufacturer and are set at installation. Each day the integration window, which must be symmetrically positioned about the lead peak, is verified and, if necessary, reset. This parameter is referred to as the integration set point.

Anticoagulants for ASV

Either heparin or EDTA may be used with the ASV method. Heparin requires no special procedures for analysis but may present a problem because of micro-clot formation, which makes the blood specimen non-analyzable. This problem most often occurs when blood specimens must be transferred from the collection site to a remote laboratory. EDTA is the preferred anticoagulant.

After the samples have been placed in tubes using a pipette, they should be incubated for 15-30 minutes before proceeding with the analysis. If standard evacuated glass tubes containing EDTA are used to collect blood, then the tubes must be at least half-full before the samples can be analyzed because, if the concentration of EDTA exceeds the usual 1.5 mg/mL, decomplexation of the lead is reduced, and the level of lead determined will be falsely low.

Calibration

When direct determination of lead levels in blood is performed by ASV (i.e., without acid digestion), calibration with aqueous lead standards is not possible, nor is it possible to use lead-spiked blood, since there are subtle differences between whole blood containing

endogenous lead and whole blood spiked with inorganic lead. The instrument should be calibrated with blood-based materials traceable to the National Institutes of Standards and Technology (NIST) or to another well-characterized reference material. Blood-based calibrators may also be purchased commercially, prepared by the laboratory with the assistance of a reference laboratory, or they may be provided, along with the reagents, by the instrument manufacturer.

One reference laboratory with successful experience using ASV reports that calibration is most accurate if human blood, with endogenous lead levels that have been established by thermal ionization mass spectrometry (TI-MS), is used (J. Chisolm, M.D., Kennedy Krieger Institute, personal communication, 1993). Certainly, other ASV reference laboratories[16] would also agree that success with determining blood lead levels depends on routinely checking instrument calibration with independently-validated blood-based reference materials, such as the Standard Reference Material (SRM) 955a Lead in Blood from NIST, the CDC Blood Lead Laboratory Reference System (BLLRS) pools, or New York State's lyophilized reference material for blood lead determinations.

Another concern for ASV users is a potential interference from copper, which is oxidized or stripped at a potential close to that for lead.[16] Since copper is an essential element and is present in human serum in detectable amounts, the possibility exists for an interference, especially in populations where serum copper levels are elevated (e.g., in pregnant women). This interference is minimized by properly selecting the integration set point and using the currently recommended instrument parameters. Some laboratories use a strip-chart recorder to check for problems with copper interference.

Other electrochemical methods for measuring blood lead levels

Recent developments in analytical instrumentation have led to the development of prototype instruments for determining lead levels in blood by potentiometric stripping analysis (PSA), an electrochemical technique similar to ASV. Although not yet commercially promoted for measuring blood lead levels, PSA has been used successfully.[17,18] In addition, other electrochemical technologies are currently under development with the goal of providing a relatively inexpensive and portable means of screening children for lead poisoning.

Quality Assurance and Quality Control in the Clinical Lead Laboratory

Quality assurance and quality control can be loosely defined as those aspects of laboratory policy and practice which ensure that all test results are reported accurately. Although it is not possible to give a comprehensive description of all QA/QC practices, some aspects that are considered desirable for the clinical lead laboratory are given below. Under the 1988 Clinical Laboratory Improvement Act (CLIA) regulations, all clinical laboratories in the United States are required to document those aspects of tests considered of moderate or high complexity (Subpart K of 57 CFR 493), including the need to establish and verify method-performance specifications. These test aspects include accuracy, precision, reportable range, and analytical detection limit.

Control procedures

Under 1988 CLIA regulations, control procedures should be in place that monitor instrument stability and operator variance for all quantitative tests, and a daily QC procedure should be performed that includes at least two samples of different concentrations (normal and abnormal) to ensure the ongoing validity of test

results (§493.1218). For blood lead measurements, the clinically relevant concentration range is 5 to 100 μg/dL of whole blood although confirmed blood lead concentrations above 70 μg/dL are rare. Most analytical methods are calibrated for a working range of up to 60 μg/dL, with dilution required for specimens that are above the highest calibration point. Most modern GFAAS methods have detection limits that are significantly better than 5 μg/dL and can, therefore, report test values of less than 5 μg/dL.

For daily QC monitoring, a variety of materials are available for blood lead measurements. (See Appendix B.2.) We caution laboratories to verify independently each batch of daily QC materials against a certified reference material before they are used routinely. Any large deviation (1-2 μg/dL) from the stated target value warrants further investigation.

The acceptable range for routine daily QC should be no greater than that allowed for PT performance samples (i.e., ± 4 μg/dL or ± 10%, whichever is greater). Most laboratories experienced in analyzing blood lead levels should have no difficulty in achieving a day-to-day precision that is better than ± 4 μg/dL at values of 10 μg/dL. Therefore, CDC's Advisory Committee on Childhood Lead Poisoning Prevention recommends that, for investigative actions, laboratories set their internal QC limits to ± 2 μg/dL or ± 10%, whichever is greater.

Although 1988 CLIA regulations require a minimum of only two control concentrations (normal and abnormal) for blood lead measurement, the Advisory Committee also recommends that at least three levels of QC be employed at low ($\leq$ 10 μg/dL); intermediate (25- 30 μg/dL) and high (40-60 μg/dL) calibration ranges for blood lead levels. The rationale for this recommendation is that most daily QC problems with blood lead measurements arise with the use of the high-level control (> 40 μg/dL) because of sensitivity drift. If the blood lead level of a single high-level control (50 μg/dL) is out of the acceptable range, but the low-level control (10 μg/dL) is within range, then all test results in the batch (e.g. tray, carousel) that are greater than the upper limit blood lead level of the low-level control (i.e., > 14 μg/dL) would have to be rejected and the specimen(s) reanalyzed. This reanalysis may create a problem if, for example, the rejected results were capillary specimens, and there was not enough sample remaining to perform a repeat analysis.

Under current regulatory guidelines, test results above the upper limit of the lead level of the low-level control can not be reported and the laboratory would request that another specimen be obtained. Had an intermediate control (30 μg/dL) been included in the run, the outcome might have been different. For example, an intermediate control might have been within acceptable limits, albeit with a low bias, but would have enabled the laboratory to report the results of testing a capillary sample (e.g., results between 14-34 μg/dL) without having to obtain another specimen.

Another reason for the tri-level approach is that with ASV analysis, when the electrode plate begins to thin, the higher blood lead values begin to lose accuracy (J. Chisolm, M.D., Kennedy Kreiger Institute, personal communication, 1993). Similarly, with GFAAS analysis, the most common problem is associated with unacceptable errors with high-level control values (i.e., values > 50 μg/dL).

Clinical lead laboratory approval and accreditation

The CLIA regulations of 1988 require that all clinical laboratories performing blood lead tests participate successfully in an approved PT program. Currently, five PT programs for proficiency in blood lead testing have been

approved by HCFA for CLIA purposes (Appendix B.2). Laboratories participating in any one of three of these programs can also attain approval to perform blood lead testing from OSHA.

In addition to proficiency-testing requirements, many states require the mandatory reporting of blood lead test results. Some states have or are moving toward electronic reporting of all blood lead test results, whereas others require reporting of elevated levels only. As states move to update their definitions of elevated blood lead test results, many will require the mandatory reporting of all test results, and the most efficient means for doing so is via electronic transmission. CDC's Advisory Committee supports the concept of electronic reporting of all blood lead test results by state since doing so will facilitate CDC's efforts in monitoring the incidence and prevalence of lead poisoning nationally. For additional information on electronic reporting of blood lead testing data, please contact your state health department or CDC.

Turnaround time for blood lead test results

Laboratory turnaround time for blood lead testing will depend on several factors, including the analytical method used, work-load fluctuations, and quality control protocols used. Although most public health laboratories only operate on a 9 a.m. to 5 p.m. weekday schedule, many private laboratories operate around the clock, and therefore, may be able to reduce turnaround time considerably. What is considered a reasonable turnaround time may be differ for the different specimens that are analyzed. All laboratories recognize the need to allocate a higher priority to those specimens considered urgent (e.g., *stat* requests). However, capillary blood specimens, which are considered for screening purposes only, should be analyzed and reported to the requesting physician within 1 week of being received in the laboratory. Venous blood specimens, which are more likely to be used for confirmatory follow-up purposes, should receive a higher priority than that allocated to a screening specimen. Confirmatory specimens should be analyzed and reported within 3 days of receipt in the laboratory. For *stat* requests, the laboratory should be able to reduce turnaround time to 24 hours or less. A *stat* request to determine a blood lead level from a capillary blood specimen is inappropriate because such a request implies that the result will be used to determine a course of medical management.

Reporting blood lead results

In the United States, blood lead test results are usually reported in units of micrograms per deciliter of whole blood (i.e., μg/dL or μg/100 mL. In most other countries, the international system (SI) of units are preferred (i.e., micromoles per liter whole blood [μM or μmol/L]). To convert results in μg/dL to μM, multiply the former by 0.048; for example, 10 μg/dL = 0.48 μM.

A related aspect of reporting a blood lead value is the rounding-off of the result. The number of significant figures given is indicative of the precision of the analytical method. The convention in analytical chemistry is to report all the digits that are certain plus the first uncertain one.[19] The precision of most routine blood lead methods developed before the 1980s was only ± 1-2 μg/dL or greater. Thus, routine blood lead results were always rounded to the nearest integer for clinical purposes.

Now that the blood lead level of concern has been lowered from 25 μg/dL to 10 μg/dL of blood lead, analytical methods with improved precision have been developed for determining lower concentrations of lead in blood. For example, modern GFAAS methods can attain a between-run precision of approximately ± 0.3 μg/dL at low levels.[8] Therefore, with repeated

analyses (n > 3), blood lead test results at low levels could be reported to the first decimal with some confidence if such reporting were required (e.g., for research purposes). Of course, the laboratory would have to validate within-run and between-run precision to justify reporting results with such implied precision. For many routine blood lead testing methods, however, such precision is not justified for a single analysis; moreover, the clinical significance of such precision has not yet been established. Therefore, routine blood lead test results should still be rounded to the nearest integer.

Determining the Level of Lead in Urine

In the past, the primary purpose of determining lead levels in urine was to assess total lead excretion over a fixed period, usually 8 hours, as a function of the dose of calcium disodium ethylenedramine tetracetic acid ($CaNa_2EDTA$) given. Although using the lead mobilization or "provocation" test has decreased in recent years and demand for testing urinary lead levels has dropped, laboratories continue to receive specimens for analysis. Tests for lead levels on non-timed or "spot" urine specimens are considered to have little clinical value but are still used to monitor workers occupationally exposed to organolead compounds. Some guidance and recommendations for determining the level of lead in urine is provided below.

Recommended procedure for collecting urine samples

Collecting urine for a provocation test is almost always performed on an inpatient basis, and with very young children some additional difficulties occur in ensuring that the entire 8-hour specimen is collected without contamination from exogenous lead. A special commercially-available plastic pouch is taped over the child's genitalia to facilitate urine collection. However, it is the responsibility of the laboratory providing the analysis to ensure that all materials used to collect and transport urine specimens are lead-free.

For an 8-hour urine collection, the laboratory should provide a supply of primary urine collection containers (1-L volume) with caps, preferably plastic. Containers should be certified as lead-free, either by acid-washing them with 2% (v/v) nitric acid for 24 hours, followed by washing them with deionized water, or by selecting a small number from a batch, filling them with 2% nitric acid, and analyzing the leachate for lead. Either of these procedures should prevent the use of contaminated containers.

Transporting or shipping urine specimens to centralized laboratories

If the urine lead test is to be sent to a reference laboratory for analysis, then some consideration should be given to packaging and shipping the specimen. The laboratory performing the analysis should always be consulted because it may have specific requirements or employ a courier service. Generally, it is unnecessary and cumbersome to ship the entire urine specimen for analysis since the cost will be higher and risks for leakage greater. A 10-mL aliquot is usually sufficient for analysis, and this aliquot can be easily transported in commercially available plastic syringes designed specifically for transporting urine specimens.

There is no need to refrigerate urine specimens during transit since they are quite stable for several days. All urine collection materials should be provided by the testing laboratory and certified as lead-free.

Using additives as stabilizers

For determining lead levels in urine, some laboratories have proposed stabilizing the specimen with dilute nitric acid. However, the

justification for acidification is weak, and addition of acid provides an opportunity to contaminate the specimen. Lead at high concentrations might precipitate out of solution at a pH of 6-7, but this is hardly the case with urine, where the pH is much lower. For this reason, it is unnecessary to add nitric acid to the specimen.

Analytical Methods For Determining Lead levels In Urine

Most laboratories use GFAAS to determine lead levels in urine; ASV may also be used for the direct determination of urine lead levels, but analyzing urine by ASV requires different treatment than analyzing blood by ASV. When using GFAAS, the urine lead analysis can be more troublesome than that for blood lead because of the high inorganic salt content in urine and the lack of reliable urine reference materials with certified lead content at clinically relevant concentrations.

Graphite furnace AAS

For some furnace instruments, it may be possible to calibrate directly with aqueous lead standards. If this is not possible, the best approach is to calibrate with matrix-matched standards (i.e., with lead-spiked urine containing nitric acid (2% v/v) and $NH_4H_2PO_4$ modifier). A donor should be sought who can provide urine samples containing little or no detectable lead. Typically, the calibration range for urinary lead is 0 - 60 μg/L, as it is for blood lead. Because human urine can vary considerably, a 1+9 dilution with modifier/acid will help offset any potential interferences from other components present. As a rule of thumb, the analysis should always be approached by referring to the STPF concept.

Anodic stripping voltammetry

ASV can be used to determine urine lead levels, but several modifications are required for this analysis to be successful. First, calibrators specific for measuring urine lead levels should be used, and some laboratories recommend that nickel be incorporated into the supporting electrolyte/decomplexing solution to facilitate displacement of lead from EDTA (J. Chisolm, M.D., Kennedy Kreiger Institute, personal communication, 1993).

Quality Assurance and Quality Control

Few reliable reference materials exist specifically for QA/QC of urine lead measurements. NIST provides a bi-level Toxic Metals in Human Urine material (SRM 2670) that is certified for lead at an “abnormal” level of 109 μg/L, and a low level of 10 μg/L is given for informational purposes. However, this material has only limited application for clinical purposes, where typical urine concentrations range from 50 to 1000 μg/L. Using a 1+9 sample dilution, a linear calibration range up to 60 μg/L gives directly reportable concentrations of up to 600 μg/L. Clearly, there is a need for reliably validated urine lead reference materials at concentrations between 100 and 600 μg/L. A list of urine control-material sources is provided at in Appendix B.2.

Performance criteria for analyzing lead in urine

There are no established performance criteria for analyzing urine lead levels. Currently, no proficiency testing exists specifically for urine lead because the test is so rarely performed. Nonetheless, it should be possible for analytical laboratories to achieve a level of performance of $\pm$ 60 μg/L at concentrations of < 400 μg/L and $\pm$ 15% at concentrations above 400 μg/L. In fact, these were the performance standards expected for blood lead determinations before 1991, and

they reflect the actual performance of a group of laboratories performing urine lead determinations using GFAAS, ASV, and MIBK-FAAS.[20]

Erythrocyte Protoporphyrin Test

The erythrocyte protoporphyrin (EP) test was used for many years throughout the United States as a screening test to identify children exposed to lead. In the 1991 edition of *Preventing Lead Poisoning in Young Children*, CDC recommended that EP no longer be used as a screening test to detect lead-exposed children.[21] The justification for this recommendation was that the results of numerous studies showed the poor diagnostic sensitivity of EP for detecting blood lead levels at 10 μg/dL, and even at 25 μg/dL, coupled with an equally poor specificity.[22,23]

However, EP remains a valuable test in the medical management and follow-up care of children with confirmed elevated blood lead levels and as a screening test for iron deficiency. Blood lead-EP pairs are particularly useful in following long-term trends in lead absorption and in evaluating the question of internal redistribution of lead after chelation therapy.

Specimen collection

Either capillary or venous blood may be used for the EP test; however, blood specimens should be protected from prolonged exposure to light. For example, evacuated glass tubes can be wrapped in aluminum foil. The preferred anticoagulant for this test is EDTA, although heparinized blood may also be used. Instructions on capillary collection are given in Appendix B.2

Analytical Methods For Determining EP

There are two principal methods for determining EP, acid-extraction and hematofluorometry. The extraction method is generally accepted as the reference method for EP and involves extracting protoporphyrin and other heme components from whole blood into a mixture of ethyl acetate and acetic acid and "back-extracting" the protoporphyrin into dilute hydrochloric acid. Quantitation is performed using a spectrofluorometer calibrated with protoporphyrin IX standards. A complete description of the extraction method is beyond the scope of this document; refer to the National Committee for Clinical Laboratory Standards' (NCCLS) document CP42-P on Erythrocyte Protoporphyrin testing.[24]

Hematofluorometry (HF) uses a small portable fluorometer dedicated specifically to measuring EP directly in whole blood as the zinc chelate, zinc protoporphyrin (ZPP). This instrument was once widely used in public health programs to screen children for lead exposure. Again, a complete description of the use of and issues related to hematofluorometry is beyond the scope of this document; referred to the NCCLS document on EP testing mentioned above.

Millimolar Absorptivity (mϵ) of Protoporphyrin IX

One issue yet to be completely resolved is continued widespread use of an incorrect millimolar absorptivity (mϵ) value (241 L cm^{-1} $mmol^{-1}$) for protoporphyrin IX calibration standards. Since most hematofluorometers trace calibration back to the reference extraction method, the mϵ issue affects hematofluorometry as well. Historically, the mϵ value was thought to be 241 L cm^{-1} $mmol^{-1}$, but this value has been recently shown to be incorrect and the true value is 297 L cm^{-1} $mmol^{-1}$.[25] The impact of using the correct mϵ value is a 19% decrease in all EP test results, including reference ranges. However, individual laboratories in the United States should not initiate any changes in calibration procedure unilaterally but should follow directives from the Health Resources and Services

Administration (HRSA)-sponsored PT program for EP, operated by the Wisconsin State Laboratory of Hygiene, and from state PT programs for EP because such changes will have an impact on hematofluorometer calibration, target values for standards and controls, and reference ranges for EP.

Reference ranges for EP

In the 1985 edition of *Preventing Lead Poisoning in Young Children*,[26] CDC adopted an EP value of 35 μg/dL of whole blood as the upper limit of normal for screening children for lead exposure. This level corresponded to a blood lead level of 25 μg/dL. A simple adjustment of that value, correcting for the m$\in$ error, results in a lower value of 28 μg/dL, which was adopted in the 1991 edition of *Preventing Lead Poisoning in Young Children*.[21] The NCCLS document on EP testing reports the correct upper limit of normal for EP, using m$\in$ of 297 L cm^{-1} $mmol^{-1}$, to be 30 μg/dL, partly on the basis of reanalysis of the NHANES II data set, for which EP values were originally determined using an m$\in$ value of 297 L cm^{-1} $mmol^{-1}$.[24] Thus, the CDC Advisory Committee, recognizing that EP has been plagued by historical inaccuracies in the analysis, recommends that the upper limit of normal for an EP test result is 30 μg/dL of whole blood. However, the Advisory Committee also reiterates that individual laboratories should follow guidance from PT program officials on the timing and manner in which this change in calibration should occur.

Standards and control materials for EP testing

The availability of standards and control materials for use in determining EP is limited. Pure protoporphyrin IX standards are available from only one source (Porphyrin Products, Logan, Utah). For extraction methods, lyophilized whole blood control materials are available from several sources and have been used as either control specimens or as secondary standards. Frozen whole-blood materials (human, bovine, or goat), if properly stored and protected from light, may also be used but are not commercially available. Hemolyzed or reconstituted lyophilized blood cannot be used with hematofluorometry because it requires the presence of intact red blood cells for correct quantitation. Since HF calibration is usually provided by the manufacturer, daily quality control is limited to testing liquid blood materials manufactured specifically for the hematofluorometer (Appendix B.2).

Proficiency testing programs for EP

A limited number of PT programs are available for EP. They include the HRSA-sponsored program operated by the Wisconsin State Laboratory of Hygiene that is open to anyone and several state-based PT programs (e.g., in New York, Pennsylvania, and New Jersey), where participation is required for in-state permit purposes. (See Appendix B.2.) Although participation in a PT program for EP is not required by HCFA under the 1988 CLIA regulations, the Advisory Committee strongly recommends that all laboratories performing the analysis for EP participate successfully in such a program.

Miscellaneous Tests For Lead In Biological Fluids or Tissues

Lead levels can be determined in a number of different tissues (teeth, hair, nails) and body fluids (breast milk, sweat, plasma). However, the clinical utility of such analyses is doubtful, and some tissues (e.g., hair, nails), may be so grossly compromised by contamination errors as to make their analysis totally unreliable. Tests to determine lead levels in teeth have proven useful in clinical research studies,[26,27] because they reflect cumulative lead exposure but are less valuable as routine clinical tests. Teeth may not

always be available for specimens and may be compromised by inappropriate storage. The analysis is complicated by the fact that the tooth specimen must be "digested" under clean conditions before its lead content can be measured.

Digestion techniques are not routinely practiced by most clinical laboratories. No reference materials or controls are available to validate such analytical procedures and, given the regulatory requirements of CLIA, many laboratories capable of performing the analysis are reluctant to offer it because of such obvious difficulties. The same difficulties hold true for tests for lead levels in milk, hair, and nails.

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Estimated Prevalence in sample	Number Screened	95% confidence intervals[2] lower	upper
	400	9%	15%
	1000	10%	14%
14%	50	6%	27%
	100	8%	22%
	200	10%	20%
	400	11%	18%
	1000	12%	16%
16%	50	7%	29%
	100	9%	25%
	200	11%	21%
	400	13%	20%
	1000	14%	18%
18%	50	9%	31%
	100	11%	27%
	200	13%	24%
	400	14%	22%
	1000	16%	20%
20%	50	10%	34%
	100	13%	29%
	200	15%	26%
	400	16%	24%
	1000	18%	23%
25%	100	17%	35%
	200	19%	31%
	400	21%	29%
	1000	22%	28%
30%	50	18%	45%
	100	21%	40%
	150	23%	38%
	200	24%	37%
	400	26%	35%
	1000	27%	33%
40%	50	26%	55%
	100	30%	50%
	200	33%	47%
	400	35%	45%
	1000	37%	43%
50%	50	36%	64%
	100	40%	60%
	200	43%	57%
	400	45%	55%
	1000	47%	53%

[1] These confidence intervals are calculated on the basis of the binomial distribution, which assumes that the children are drawn from an infinite population. This assumption is appropriate for making predictions about a population of undefined size that may be tested over time. However, these confidence intervals do not apply if, for example, the whole population of interest has been tested.

[2] Rounded to the nearest whole number.

Table 1. Expected Proportions of Children with BLLs Higher Than Selected Thresholds, Given Different Prevalences of Elevated BLLs.

Geometric Mean	Percentage ≥ 10 μg/dL	Percentage ≥ 15 μg/dL*	Percentage ≥ 20 μg/dL†	Percentage ≥ 25 μg/dL‡
2.2	1%	0.2%	0.03%	0.009%
2.7	2%	0.4%	0.09%	0.025%
3.5	5%	1.1%	0.32%	0.106%
3.9	7%	1.8%	0.53%	0.185%
4.4	10%	2.8%	0.91%	0.337%
4.9	13%	3.9%	1.37%	0.533%
5.0	14%	4.3%	1.54%	0.607%
5.8	20%	7.0%	2.73%	1.163%
6.4	25%	9.6%	3.97%	1.777%
7.1	30%	12.4%	5.43%	2.547%
8.5	40%	18.8%	9.12%	4.639%

* Rounded to the nearest tenth of a percent.
† Rounded to the nearest hundredth of a percent.
‡ Rounded to the nearest thousandth of a percent.

Introduction

Despite considerable progress in controlling lead exposure in the United States, 9% of American children have elevated blood lead levels (BLLs), that is, BLLs of at least 10 micrograms per deciliter (μg/dL). Some of these children have higher BLLs.[1] Very high BLLs are associated with a variety of severe health effects; subtle problems with learning and behavior have been reported among children with BLLs at least as low as 10 μg/dL.[2] Screening children for elevated BLLs to trigger interventions to reduce lead exposure is one of many tools for preventing or controlling childhood lead poisoning.

In 1991, the Centers for Disease Control (CDC) recommended screening all children for elevated BLLs, except in communities where large numbers or percentages of children have been screened and found not to have lead poisoning.[3] In some communities, the resultant increase in screening helped to identify large numbers of children with elevated BLLs who needed individual management to reduce their BLLs.[4,5] However, average BLLs U.S. children have declined,[1] and some communities have identified relatively small numbers of children with elevated BLLs, a finding that has prompted considerable concern about whether universal screening for elevated BLLs provides benefits that outweigh its risks and costs.[6,7]

A quantitative comparison of the costs and benefits of universal screening for elevated BLLs (universal screening) at varying prevalences of elevated BLLs may now be useful for two reasons. First, it can serve as a basis for guidance about screening in populations with different prevalences of elevated BLLs. Second, it may help to define areas where research is needed into the effectiveness and cost-effectiveness of BLL screening.

Methods

Structure of the simulations

We used mathematical simulations of a BLL screening program to compare the estimated economic costs and benefits of performing universal screening for elevated BLLs compared with performing no screening in hypothetical populations of 10,000 1-year-old children with different prevalences of elevated BLLs. For each population, we estimated the following (Figure 1):

1. A distribution of "true" BLLs among the children.
2. The BLLs observed among children in a screening program.
3. The costs of screening, follow-up, and interventions to reduce children's BLLs.
4. The effectiveness of interventions triggered at age one to reduce children's BLLs at age 2.
5. The health and economic benefits that might result later in life as a result of reducing children's BLLs at age 2.

Data and assumptions

We obtained data for the simulations by reviewing published and unpublished studies and by consulting with experts in lead poisoning prevention, epidemiology, pediatrics, public health, and economics. When necessary, we contacted authors of published studies for additional data that do not appear in the published reports. We chose a single best estimate and a range of uncertainty for every assumption.

Economic assumptions

The analysis was done from a societal perspective (i.e., we attempted to include all costs and benefits of screening without regard to who would pay the costs or receive the benefits). We adjusted economic costs and benefits to 1992 dollars using the Consumer Price Index for all items (CPI) or the medical CPI and also adjusted wages to 1992 dollars using the

estimated annual hourly earnings growth for the nonfarm sector.[8] We discounted economic costs and benefits occurring in the future at 5% per year.

Distribution of BLLs in the population and performance of screening tests

Information about the distribution of BLLs in the population and the performance of BLL screening tests are summarized in Table 1. We defined distributions of true BLLs in children and changed the prevalence of elevated BLLs by changing the geometric mean of the distribution.

BLLs measured in a screening program can be either falsely high or falsely low compared with true blood lead levels because laboratory measurement of BLLs is not perfectly accurate or precise. We accounted for errors and biases in blood lead measurement from three sources: biases due to blood-sampling techniques, imprecision in laboratory measurement of BLLs, and changes in children's BLLs with time.

We assumed that screening blood samples were obtained by fingerstick and that confirmatory and follow-up samples were obtained by venipuncture. Because BLLs obtained by fingerstick may be contaminated by lead on the child's skin, we assumed that the laboratories overestimated "true" BLLs by an average of 1μ g/dL.[9,10] We assumed that specimens obtained by venipuncture did not have a systematic bias.

We estimated the variability in children's BLLs from imprecision in laboratory testing and variability in children's BLLs with time by using data from research studies in which children's BLLs were repeatedly measured. These studies allowed us to estimate the geometric standard deviation (GSD) of each log-transformed BLL (the within-individual GSD). We used this value to randomly simulate screening, confirmatory, and follow-up BLLs that would be observed in a screening program in which the observed BLL = $e^{[\ln(\text{"true" BLL at age one})+(\ln(\text{within individual GSD}))*\text{random term}]}$ and the random term was normally distributed with a mean of zero and variance of one.

This method allows us to account for blood lead testing results that are either higher than the true BLLs (false positive) or lower than the true BLLs (false negative). False positive results generate costs out of proportion to benefits, and false negative results may result in a failure to obtain some of the benefits that would otherwise have been expected from the screening program.

The observed GSD (antilog of the standard deviation on the log scale) in the simulated screening test results was 1.9—higher than the range of 1.67-1.79 reported in several recent studies of children living near lead smelters.[11] We chose this value because children living near smelters probably have less than typical variability in BLLs since all such children share a single large source of lead exposure. In contrast, we selected values so that the "observed" GSD in our simulations was less than the 2.12 recently measured in a probability sample of U.S. children in the Third National Health and Nutrition Examination Survey (NHANES III)[1] **(and CDC, unpublished data, date ?)** because the national estimate includes variability among communities that is not relevant in any single community.

Costs of Screening and Interventions

The cost estimates used in this analysis and the ranges for sensitivity analyses are shown in Table 2.

Screening and follow-up services

A visit to a physician and a blood sample for anemia screening are recommended for 1-year-old children whether or not BLL testing is done.[12] For children whose observed BLLs are not elevated, no additional follow-up care is recommended, and the laboratory cost of a blood lead test represents the entire cost of screening.

For children with elevated BLLs, additional blood lead testing is recommended. We assumed that children with screening BLLs of at least 10 μg/dL would require one confirmatory and one follow-up BLL test and that children with BLLs of at least 20 μg/dL would require a confirmatory and two follow-up tests. The cost of each recommended confirmatory and follow-up test included the costs of a visit to a pediatrician, a venipuncture, and a BLL test.

We assumed that children with elevated BLLs received education about lead poisoning and environmental and medical management.[3] Children were assigned these services on the basis of confirmatory BLL results.

Families of children with confirmed elevated BLLs were assumed to receive education about lead poisoning and ways to prevent it. Available studies that estimate the effectiveness of education in reducing BLLs involved home visits by study personnel. Therefore, we assumed that home visits would occur and assigned costs and benefits accordingly.

In our simulations, children with confirmed BLLs of at least 20 μg/dL or two consecutive BLLs exceeding 15 μg/dL received environmental assessments and interventions (environmental management) in addition to education. The environmental management on which benefits were based in our simulations involved house cleaning and spot-paint repair.[13] We evaluated changing the cost and effectiveness of these interventions in sensitivity analyses.

In our simulations, children with BLLs of at least 40 μg/dL but less than 70 μg/dL received outpatient medical treatment with the oral lead-chelating drug succimer, as well as education and environmental management. Children with confirmed BLLs of at least 70 μg/dL received in- hospital treatment with intravenous edetate disodium calcium (EDTA). Chelation therapy is sometimes used for children with BLLs as low as 20 μg/dL,[14,15] so we evaluated changing BLL ranges for which chelation would be used in sensitivity analyses.

We assumed that half of the children who received chelation therapy with EDTA required two courses, that one-quarter of the children required three courses,[16] and that the average number of chelation treatments with succimer was similar to that required with EDTA. We assumed that all repeat courses of chelation therapy used succimer. Thus, each child requiring EDTA received an average of one course of EDTA and 0.75 courses of succimer, whereas each child receiving succimer received an average 1.75 courses.

Side effects of chelation therapy are generally minor and rare.[3] We did not assign costs associated with treating these side effects.

Direct nonmedical costs

We estimated that both clinic visits and environmental interventions required 2 hours of one parent's time and that a home education visit required 1 hour of one parent's time. We did not assign a time cost for chelation therapy because we are unaware of available data allowing us to estimate this cost and because few children undergo chelation therapy. Thus, this cost would have little effect on the simulations. We estimated the cost of parents' time on the basis of the U.S. mean daily wage.

Benefits of screening

The objective of BLL screening is to identify children with elevated BLLs so that educational, environmental, and medical therapy can lower their BLLs and improve their health outcomes. For this analysis, we estimated the health and economic benefits of screening by estimating 1) the number of children with elevated BLLs who would not have been identified without screening, 2) the reductions in BLLs that could be achieved by educational, environmental, and

medical interventions, and 3) the health and economic benefits of reducing BLLs. We have attempted to place an economic value on the following benefits of reduced BLLs: improved learning and behavior, lower special education costs, benefits of identifying and fixing lead hazards in housing.[17]

Expected BLLs in the absence of screening
BLLs in children typically increase from age 1 to age 2.[18] To predict these expected increases, we used data from the Cincinnati cohort study in which the ratio of children's geometric mean (GM) BLLs at age 2 to those at age 1 stratified by housing type ranged from 1.16 to 1.29[18] (S. Clark, University of Cincinnati School of Medicine, Department of Environmental Health, personal communication, 1994). We chose 1.19 as our base estimate of this value.

Individual children have BLL increases with age that vary around this average. We estimated 1) each child's expected BLL at age 2 as a function of the "true" BLL at age 1, 2) the average increase in children's BLLs from age 1 to age 2, and the within-individual standard deviation of children's BLLs at age 2 using this equation: $e^{[\ln(\text{"true" BLL at age one})+1.19+(\ln(\text{within-individual GSD}))*\text{random term}]}$.

We estimated the within-individual standard deviation as 1.33 on the basis of changes in children's BLLs from age 1 to age 2 in the Cincinnati cohort study[18] (P. Succop, University of Cincinnati School of Medicine, Department of Environmental Health, personal communication, 1994). The random term was normally-distributed with a mean of zero and a variance of 1. We applied changes in BLLs attributable to interventions to the expected BLL at age 2.

Effectiveness of interventions in reducing BLLs
Estimates of the effectiveness of interventions in reducing children's BLLs are summarized in Table 3.

Education
Our "base-case" estimate of education's effectiveness in reducing BLLs came from Milwaukee Health Department program data. These data were collected from children whose initial BLLs ranged from 20 to 24 μg/dL, and most follow-up blood lead data were collected from 3-12 months after the initial BLL. After adjusting for season, researchers found that children whose parents received education about lead poisoning prevention had follow-up BLLs that were 0.87 times the BLLs of children whose parents did not receive education. This estimate varied little with the increasing time interval between the initial and follow-up BLL test.[19]

We assumed that this reduction in exposure would apply to all children who received educational visits and had true BLLs of at least 20 μg/dL. We assumed that children who had true BLLs of less than 20 μg/dL had no change in BLLs after their parents had received educational information about preventing lead poisoning.

An alternative estimate of the effectiveness of education in reducing children's BLLs came from a study done in a community located near an Illinois lead smelter.[20] In this study, families of children with elevated BLLs received intensive education. Children whose families had the intervention had average follow-up BLLs of 0.64 times their initial BLLs[20] (and R. Kimbrough, The Institute for Evaluating Health Risks, Washington, D.C., personal communication, 1995). This study did not incorporate a control group and probably overestimated the effectiveness of education for at least two reasons: first, it did not account for regression to the mean (i.e., it did not account for the tendency of subjects with extreme values of a test to have scores closer to the mean on

retesting). Second, it did not account for the effect of aging of the children on BLLs (i.e., it did not account for the fact that older children have lower average BLLs than younger children). For these reasons this study represents a ceiling estimate of education's potential effectiveness. We used this estimate in a sensitivity analysis for children with true BLLs of at least 10 μg/dL. For a lower-bound estimate of the effectiveness of education, we assumed education had no effect on BLLs.

Environmental management
We used data from a study in St. Louis, Missouri, to estimate the effect of environmental management on BLLs.[13] One year after house cleaning and spot-paint repair, children in the intervention group whose initial BLLs ranged from 25 μg/dL to < 35 μg/dL had BLLs that were 0.99 times those in the control group. Children whose initial BLLs were at least 35μg/dL had BLLs of 0.79 times those among children in the control group. In base-case analyses, because of the limited effectiveness of this intervention for children with lower initial BLLs, we did not assume that this environmental intervention reduced BLLs for children with true BLLs < 25 μg/dL.

We did not find other controlled studies measuring the effect of environmental interventions on children's BLLs although several such studies are in progress. We expect that more extensive interventions would result in greater reductions in children's BLLs but would be more expensive. We tested the effect of increasing the costs and the effectiveness of environmental management in sensitivity analyses.

Chelation therapy
The goal of chelation therapy is to permanently reduce a child's BLL to < 25 μg/dL.[14,21] In our simulations, we assumed that the combination of chelation therapy, environmental management, and education could reduce the BLLs of children receiving chelation therapy to 20 μg/dL by age 2. We did not evaluate the effects of chelation independently from the effects of other interventions because chelation therapy should always be done in conjunction with education and environmental management.[3]

Health benefits of reducing BLLs
We have used the established inverse relationship between children's BLLs and their full-scale IQ to estimate the adverse health effects of elevated BLLs because this relationship between BLL and IQ is consistently reported in most studies and has been well quantified by meta-analyses. For a base-case analysis, we used the results of a recent meta-analysis that showed that a 1 μg/dL increase in BLL at age 2 results in a loss of 0.257 points of IQ at school age.[22] In sensitivity analyses, we present the results of using another recent meta-analysis that has estimated that a 1 μg/dL increase in BLL at age 2 results in a loss of 0.185 points of IQ at school age,[23] and we also show the results of varying the range of assumptions more widely.

Economic benefits of reducing BLLs
Estimates of the economic benefits of reducing BLLs have been published previously.[16,17] Estimates of economic benefits of reduced lead exposure used in this analysis include three main categories: 1) improvements in lifetime earnings attributable to reductions in lead-induced problems with intelligence or behavior, 2) reduction in lead-related special-education costs, and 3) economic benefits of identifying and fixing dangerous housing so that other people are not exposed to lead. A complete review of this topic is beyond the scope of this discussion, but these valuation methods have been discussed in detail.[17]

Lifetime earnings
In this analysis we used reductions in lifetime earnings as a proxy for the economic costs of continuing lead exposure for children. It has

been suggested that lead exposure may reduce lifetime earnings by three pathways.[16,17] First, increased BLLs cause declines in IQ,[22,23] and reduced IQ is associated with lower wages and earnings.[17] Next, even after adjusting for lead's direct effect on IQ, researchers suggested that children with elevated BLLs may progress less far in school.[17] This reduced scholastic achievement is assumed to be mediated by the non-IQ effects of lead on development, such as reduced attention or worsened behavior. Reduced final grade achieved also directly reduces wages and may also reduce lifetime participation in the work force; both of these factors can also reduce lifetime earnings.[17] Estimates of the size of these effects are presented in Table 4. Combining these effects, we estimate that a 1μg/dL reduction in a child's BLL at age 2 compared with the BLL that would otherwise have occurred, would result in an average $1169 increase in lifetime earnings discounted to the present.

Reductions in special education costs
The cost of 3 years of special education for one child was estimated to be $18,780.[17] Assuming that 20% of children prevented from exceeding a BLL of 25 μg/dL will avoid special education that they otherwise would have required[17] and discounting special-education costs to 4 years in the future (i.e., when the child begins school), we estimate a benefit of $3090 in special-education costs saved per child who is prevented from having a BLL $\geq$ 25 μg/dL.

Primary prevention benefits
As with some other prevention activities, such as screening for sexually transmitted diseases, BLL screening may benefit people other than the person who is screened. This benefit occurs if BLL screening leads to identifying and remediating environmental lead sources, thus preventing future exposure of other people.

A previous analysis has estimated the primary prevention benefits of reducing lead in housing stock (i.e., the benefits of reducing lead exposure associated with housing that accrue to future inhabitants of a home).[16,] We have updated that model to make it consistent with current average BLLs on the basis of data from NHANES III and have assumed that the duration of the environmental management methods similar to those used in this study that involve house cleaning and spot-paint repair, is for 1 year rather than for the life of the house. We estimate a primary prevention benefit of this level of environmental management that is $745 per house that has undergone such an intervention.

Sensitivity analyses
We performed sensitivity analyses in which we varied each of our assumptions (including assumptions about distribution of BLLs in the population, performance of screening tests, effectiveness of interventions, costs, and benefits) one at a time within broad ranges.

Statistical testing
The primary purpose of this analysis was to estimate the prevalence of elevated BLLs at which the economic benefits of screening exceeded the economic costs (i.e., the prevalence at which the ratio of benefits to costs exceeds 1). After developing the final simulation, we performed replicate analyses with different random numbers to evaluate the sensitivity of the simulation to sampling error. At benefit/cost ratios near 1, the coefficient of variation (ratio of the standard deviation to the mean) of the benefit/cost ratio is approximately 5%. Thus, our estimates are relatively insensitive to sampling error, and we do not present additional measures of statistical variability.

Results
Table 5 shows estimates of the cost, effectiveness, and economic benefit of a universal screening program compared with the costs to society of having no program.

As the observed prevalence of elevated BLLs increases, both costs and benefits of universal screening increase. At low prevalences of elevated BLLs, the costs exceed the benefits. At higher prevalences, the benefits of universal screening exceed the costs. The benefits of universal screening first exceed the costs at a prevalence of 14%.

Sensitivity analyses

Results of sensitivity analyses are shown in Table 6. Changing most assumptions within broad ranges resulted in changes in the threshold prevalence at which benefits exceeded costs within a relatively narrow range of 11% to 17%. However, the simulations are very sensitive to estimates of education's effectiveness in reducing BLLs. The range of estimated educational effectiveness in reducing BLLs that we tested resulted in threshold prevalences from as low as 1% to as high as 25%. The simulations are also moderately sensitive to 1) estimates of the variability of lead exposure in the population (as measured by the population GSD), 2) biases in capillary sampling, 3) high-cost laboratory tests, 4) the cost and effectiveness of environmental management, 5) the size of the effect of lead exposure on IQ and scholastic achievement, 6) estimates of lifetime earnings, and 7) the primary prevention benefits of reducing lead in housing.

Discussion

Childhood lead poisoning is a major preventable environmental health problem in the United States. However, childhood lead exposure is not equally distributed in the U.S. population and the appropriateness of different strategies for reducing lead exposure will differ among communities. The available tools for addressing childhood lead poisoning include reducing lead hazards in housing, reducing other sources and pathways of lead exposure, screening young children for elevated BLLs, performing surveillance for elevated BLLs, and educating families about lead hazards in the environment and how to avoid them.

This analysis compares the costs versus the benefits of screening all 1-year-old children for elevated BLLs to the costs versus the benefits of screening no children. The analysis is useful for estimating the threshold prevalence at which universal screening is likely to provide benefits out of proportion to its harms and costs. In communities where universal screening seems ineffective or inefficient for preventing childhood lead poisoning, the effectiveness and cost effectiveness of targeted screening strategies and other childhood lead poisoning prevention approaches should be explored.

Ideally, decisions about BLL screening could be based on direct information that compares the advantages and disadvantages of screening in populations of children. However, no well-designed clinical trials have evaluated the effectiveness of screening to improve children's learning or behavior over the long term. Well-designed trials to test the long-term effectiveness of screening to improve children's learning or behavior would be difficult or impossible to perform today because of substantial practical and ethical difficulties.

Despite the limitations of currently available data, screening children in high-prevalence communities seems desirable. Observational studies of BLL screening in communities with high exposures to lead have generally shown reduced lead exposure when screening programs start; some of these studies have shown declining rates of symptomatic lead poisoning, case fatality, or lead-poisoning mortality.[24-27] Educational, environmental, and medical interventions that can be triggered by screening can reduce children's BLLs.[15,20,28] On the other hand, screening all 1-year-old children in low-prevalence communities does not seem efficient, effective, or desirable.[7,29] Thus, we have used

mathematical simulations of a BLL screening program to estimate the threshold prevalence of elevated BLLs at which the benefits of a universal screening program might exceed the costs.

The simulations suggested that, in communities where at least 14% (range 11% to 17%) of 1-year-old children have elevated BLLs, universal screening for elevated BLLs may provide societal economic benefits exceeding the costs of the program as well as providing health benefits for children. The national average prevalence of elevated BLLs among 1- and 2-year-old non-Hispanic Black children is 22%.[1] The national average prevalence among 1- to 5-year-old children who are poor is 16% and among children who live in large central cities is 21%.[1]

Many local studies in both urban[30-33] and rural[34,35] areas have recently reported high prevalences of elevated BLLs in all children or in subgroups of children. These prevalences of elevated BLLs are not exactly comparable to prevalence estimates in our simulations because the children in the studies are not limited to 1-year-olds. Nonetheless, these data suggest that there continue to be many U.S. populations in which testing every child's BLL at 1 year of age may provide benefits out of proportion to the costs of a screening program.

These simulations do not result in a bright line that clearly separates communities where universal screening is indicated from those where it is not. This fact is due to limitations in the data available for this analysis, to limitations in local data that would be available for decision making (i.e., a perfect estimate of prevalence of elevated BLLs in 1-year-old children will never be available), and to the fact that policy decisions are never made on the basis of a single piece of information. Nonetheless, the results of this analysis are increasingly robust as prevalence varies from 14% in either direction**.**

The national average prevalence of elevated BLLs in children who are poor, black, and live in urban areas is 36%.[1] None of our sensitivity analyses showed the costs of universal screening to exceed the benefits at this prevalence, except for assuming a substantial increase in the cost of environmental management without any increase in effectiveness, primary prevention benefit, or the real estate value of the home.

Conversely, only two sensitivity analyses, one assuming substantial increases in the effectiveness of environmental interventions without any increase in cost, and the other a probable overestimate of education's effectiveness in reducing BLLs,[20] result in the benefits of universal screening exceeding the costs at a prevalence of 4%, the U.S. average for children who are not poor.[1] Thus, the results of this analysis will be useful for making decisions about screening, especially in communities where prevalences of elevated BLLs are not close to the threshold.

Although the simulations are robust to changes in many assumptions, changing some assumptions substantially alters the results. Some variables that make universal screening less cost-beneficial can be avoided by the people performing the screening. For example, as the bias in capillary screening tests increases, universal screening is less cost-beneficial. Several studies have now demonstrated that careful technique can avoid substantial bias in capillary sampling.[9,10] Some assumptions to which the simulations are sensitive have already been reasonably well quantified. The established inverse relationship between BLL and IQ[22,23] is an example.

Other assumptions to which the simulations are sensitive demonstrate a need for better information; this is particularly true of

assumptions about the effectiveness of interventions to reduce BLLs. Many available studies of educational and environmental interventions for reducing children's BLLs did not incorporate a control group and could have overestimated the effectiveness of interventions by failing to account for changes in BLLs due to the aging of children or regression to the mean.

With the exception of a ceiling estimate of education's effectiveness in reducing BLLs,[20] our analysis used data from studies that incorporated control groups to avoid this problem. Next, much of the available information showing that interventions reduce BLLs in children came from studies where children had BLLs that were higher than are typical among children screened today. Because interventions may be more effective in reducing the BLLs of children who have higher levels than in reducing BLLs of children with lower BLLs,[15,36,37] we have not extrapolated the results of studies performed in children with higher BLLs to children whose BLLs are lower. For this reason, we assumed in base-case analyses that interventions do not reduce BLLs of less than 20 g/dL; we tested the effect of this assumption in sensitivity analyses. This assumption makes moot the continuing debates about the clinical significance of small declines in IQ related to BLLs < 20 μg/dL[22] and about whether interventions to reduce BLLs < 20 μg/dL are effective.[29]

However, if there are benefits associated with identifying individual children with smaller elevations in BLL, this analysis will have underestimated the benefits of universal screening. Although we have attempted to cope with the limitations of the available data, additional controlled studies of interventions to lower children's BLLs, especially at modestly elevated BLLs, are needed.

The results of the simulations are very sensitive to the estimated effectiveness of education in reducing BLLs because education is recommended for the parents of children with lower BLLs, and thus to the parents of many more children, than are other interventions.[3] There are conceptual reasons to believe that education could reduce BLLs by reducing exposure to lead sources, reducing exposure to lead-contaminated dust, or improving children's nutrition;[3] however, we were able to find only two studies evaluating the effectiveness of education in reducing children's BLLs.[19,20] One of these is uncontrolled.[20]

Obviously, studies that better define the effectiveness of education in reducing BLLs are needed in order to allow continuing refinement of strategies to prevent and control childhood lead poisoning.

Better studies of environmental management to reduce lead hazards in housing are also needed. The observational study used in this analysis[14] is the only available controlled study that tests the effectiveness of environmental management in reducing children's elevated BLLs. It is limited, however, because follow-up rates were low and because the environmental interventions did not conform to current guidelines.[38] More extensive environmental management results in greater and more sustained reductions in lead-contaminated dust than do less extensive interventions.[39] However, more extensive interventions are also more costly. Sensitivity analyses suggest that better environmental management methods would provide more benefit to lead-exposed children, but this larger benefit would be balanced, at least in part, by these methods' greater cost.

This analysis used methods of economically valuing reductions in lead exposure using a technique called a human capital approach; it valued reductions in BLL on the basis of improvements in lifetime earnings that might result from the lower BLLs. In general, however, people are often willing to pay more than the

cost of an illness to avoid having it entirely.[40] This potential limitation of our approach is unlikely to have substantial effect on the results at low prevalences where few people are exposed to lead and where the effectiveness of interventions to lower BLLs or improve outcomes is questionable. It may, however, result in underestimates of the benefits of screening children in communities where risk for lead exposure is higher.

We could not measure some of the noneconomic costs of screening. These include, for example, the discomfort to the child that is associated with obtaining blood samples and the potential labeling or stigmatization of some children with modest BLL elevations. These costs are likely to be small but relatively more important as the prevalence of elevated BLLs declines. Such costs seem unlikely to change substantially the results of our simulations except to further reduce the ratio of benefits to costs.

Some potential benefits of screening also could not be quantified. These fall into two general categories: 1) benefits of reducing the health or developmental consequences of lead exposure other than reduced IQ and impaired school performance; and 2) additional economic benefits of identifying and fixing dangerous housing, including improving home values and increasing energy efficiency. Especially for communities with high prevalences of elevated BLLs in children, where large numbers of children might benefit from reductions in BLLs and where large numbers of dangerous homes might be identified and fixed, our benefit calculations may be conservative. As the prevalence of elevated BLLs declines and fewer affected children and hazardous homes are identified, this underestimate will become smaller.

The analysis assumes that all children receive appropriate and timely management to lower their elevated BLLs. However, some children undoubtedly do not receive appropriate management. This lack of appropriate management has relatively little effect on estimates of the threshold prevalence at which benefits of screening exceed costs because such lack has the effect of reducing the total benefit of the program and its cost. In contrast, if appropriate interventions are delayed, benefits of screening are likely to be reduced out of proportion to costs. Although mismanagement of children with elevated BLLs may have relatively modest effects on this analysis, it has significant consequences for children and should be eliminated.

Finally, the reversibility of the adverse effects of lead exposure is open to question. The epidemiologic studies which have shown that IQ declines as BLLs increase have generally focused either on a child's BLL at age 2 or on some measure of average BLL during the preschool years as a measure of exposure to lead.[23] Screening at age 1 has been recommended[3] because early screening and interventions could reduce BLLs that would occur later compared with the BLLs that otherwise would have occurred. Thus, questions about the reversibility of lead's adverse effects may in part be mitigated by screening young children. Nonetheless, to the extent that screening is expected to reduce lead exposure that has already occurred, this analysis may have overestimated the benefits of screening. The primary prevention of lead poisoning—reducing lead hazards in the environment before children are exposed—has been successful in reducing children's exposures to lead[41] and is not subject to questions about reversibility. For this and other reasons, primary prevention of lead poisoning is preferable to screening for elevated BLLs and treating lead-poisoned children.

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Figure 1. Structure of the simulations for estimating the costs and benefits of universal screening for elevated blood lead levels (BLLs) in children.

Table 1. Population distribution of lead exposure and lead screening test performance used in an analysis of the costs and benefits of universal BLL screening.

Parameter	Estimate	Range for sensitivity analyses	Reference or rationale
Prevalence of elevated blood lead levels (BLLs)	0-50%	N/A*	Approximately consistent with the range of prevalences currently seen among children in U.S. communities.
Observed population geometric standard deviation (GSD)	1.9		See text
		1.7 to 2.12	Based on Marcus[11] National estimate based on children aged 1-5 in NHANES III† [1]
Average bias‡ of a capillary sample for blood lead	1 μg/dL		Matte[11] Schlenker et al[9] Schonfeld et al[10]
		0-2 μg/dL	Estimated
GSD of a single BLL measurement	1.27	1.17-1.43	Based on data from the Cincinnati cohort study[18]
Ratio of children's BLLs at age 2 compared with age 1	1.19	1.16-1.29	Clark et al[18]

*Not Applicable
†The Third National Health and Nutrition Examination Survey.
‡The observed value exceeds the true value by an average of 1 μg/dL.

Table 2. Cost estimates for an analysis of the costs and benefits of universal screening for elevated blood lead levels (BLLs) in children.

Parameter	Cost	Range for sensitivity analyses	Reference or rationale
Cost of a venipuncture	$7.01*		Glotzer et al[42]
		$3-$15	Estimated
Cost of a laboratory test for blood lead	$18.68*	$5.84-$87.58	Glotzer et al[42]
Cost of a provider visit for follow-up of an elevated BLL	$27.92*		Crane[43]
		$20-$50	Estimated
Direct non-medical cost of a provider visit for follow-up of an elevated BLL	$24.91†		Two hours of a parent's time at the U.S. mean daily wage
		$0-$50	Estimated
Cost of an educational visit	$51.51‡		Enterprise Foundation, 1991
		$0-$100	Estimated
Direct non-medical cost of an educational visit	$12.46†		One hour of a parent's time at the U.S. mean daily wage.
		$0-$25	Estimated
Cost of an environmental assessment	$109.75‡		Schwartz[16]
		$385‡	HUD[44] §
Direct non-medical cost of an environmental assessment	$24.91†		Two hours of a parent's time at the U.S. mean daily wage
		$0-$50	Estimated
Cost of an environmental intervention	$515‡	$515-$15,452	EnterpriseFoundation,1991§
Cost of a course of succimer	$1429†		Estimated
		$1000-	Estimated
		$4711†	Estimated inpatient cost
Cost of a course of EDTA	$4711†		Schwartz[16]
		$1000-$8000	Estimated

*Updated to 1992 dollars with the Medical Consumer Price Index (CPI).
†Updated to 1992 dollars using estimated growth in hourly wages from the Bureau of Labor Statistics.
‡Updated to 1992 dollars with the CPI.
§No lower estimate was selected for this variable.

Table 3. Effectiveness of interventions in reducing children's blood lead levels (BLLs).

Type of intervention	Ratio of children's BLLs 1 year after an intervention to those that would have occurred without the intervention	Range for sensitivity analyses	BLL Range*	Reference or rationale
Educational	1		< 20 μg/dL	U.S. Environmental Protection Agency[19]
	0.87		³ 20 μg/dL	
		1	< 10 μg/dL	Kimbrough et al[20]†
		0.64	³10 μg/dL	
		1		Assumes no effect of education for a lower-bound estimate
Environmental	1		< 25 μg/dL	
	0.99		³ 25 μg/dL and	Staes et al[13]
	< 35 μg/dL			
	0.79		³ 35 μg/dL	
		0.95-0.70	Children with confirmed BLLs of at least 20 μg/dL or persistently ³ 15 μg/dL	Estimated§
Medical (Chelation Therapy)	20 μg/dL		Initial BLLs ³40 μg/dL	Estimated
		15-25 μg/dL	Initial BLLs ³40 μg/dL	Estimated
			20 μg/dL	Initial BLLs
			³ 25 μg/dL	Estimated

*The range of true BLLs at age 1for which the effectiveness estimates were applied.
†See text for discussion.
§No estimate of lesser effectiveness was selected for this variable.

Table 4. Assumptions used to estimate the economic benefits of reducing lead exposure in children.

Parameter	Value	Range for sensitivity analyses	Reference or rationale
Reduction in IQ associated with a BLL increase of 1 μg/dL	.257 points		Schwartz[22]
		0.1-0.5	Estimated
Reduction in wages associated with each point of IQ loss	0.5%		Schwartz[17]
		0.2%	Schwartz[17]
		0.75%	Schwartz[17]
Reduction in final grade attained for each increase in lead exposure sufficient to reduce IQ by one point	0.131		Schwartz[17]
		0-0.2	Estimated‡
Reduction in wages for each one-grade reduction in final grade attained.	6%		Schwartz[17]
		4.8%-	Schwartz[17]
		8.8%	Schwartz[17]
Increased risk of failure to graduate from high school associated with an increased BLL sufficient to reduce IQ by one point	4.5%		Schwartz[17]
		0.00	Estimated‡
Reduction in workforce participation associated with failure to graduate from high school	10.5%		Schwartz[17]
		0-	Estimated
		20%	Schwartz[17]
Average lifetime earnings of a 1-year-old child discounted to the present	$266,843*		Schwartz[17]
		$200,000-	Estimated
		$500,000	
Average reduction in special education costs per child who is prevented from having BLLs exceeding 25 µg/dL.	$3090†		Schwartz[17]
		$0-$6180	Estimated
Primary prevention benefits of reducing lead in housing/per house treated.	$745		Schwartz[17]§
		$0-$2000	Estimated

*Updated to 1992 dollars using estimated growth in hourly wages from the Bureau of Labor Statistics.
†i.e., the cost of 3 years of special education discounted to the present, multiplied by the estimated 20% excess in the number of children with BLLs exceeding 25 µg/dL who will require special education.
‡No upper estimate was chosen for this variable because larger estimates can result in risks exceeding 100% at very high BLLs.
§This model has been updated for consistency with the rest of the current simulation. See text.

Table 5. Costs and benefits of universal screening for childhood lead exposure in a cohort of 10,000 children as prevalence of elevated BLLs varies for the base-case model.

Observed prevalence of elevated BLLs* (%)	Cost of the screening program†	Economic benefit of the screening program†	Ratio of benefits to costs‡
2	$230,000	$19,000	.08
5	$306,000	$69,000	.22
10	$460,000	$328,000	.71
14	$603,000	$637,000	1.05
20	$839,000	$1,236,000	1.47
25	$1,071,000	$2,002,000	1.87
30	$1,308,000	$2,919,000	2.23
40	$1,898,000	$5,693,000	3.00
50	$2,706,000	$10,328,000	3.82

*10 µg/dL, rounded to the nearest whole number.
†per 10,000 children, rounded to the nearest $1000.
‡Calculated on the basis of cost and benefit estimates that have not been rounded. The ratio may differ slightly from one calculated on the basis of rounded data from the table.

Table 6. Sensitivity of the simulations to changing assumptions for a cost-benefit analysis of universal screening for elevated BLLs in children.* Results show the threshold at which benefits first exceed costs as assumptions are changed.

Assumption	Threshold prevalenceof elevated BLLs† at which benefits first exceed costs (%)
Base model	**14**
Observed population geometric standard deviation	
= 1.7	30
= 2.12	7
Average bias of a capillary blood sample	10
= 0 µg/dL	
= 2 µg/dL	19
Cost of laboratory testing for blood lead	
= $5.84	9
= $50	22
= $87.58	27
Cost of an environmental intervention	
= $1545	19‡§
= $3502	36‡¶
= $7211	64‡**
= $15,452	89‡††
Ratio of children's BLLs after educational interventions compared to those that would have occurred without interventions.	
Based on Kimbrough et al[20]	1
Assuming that education has no effect	25

Table 6 (continued)

Assumptions	Threshold prevalence of elevated BLLs† at which benefits first exceed costs (%)
Ratio of children's BLLs after environmental interventions compared with those BLLs that would have occurred without an intervention	
= 0.90	9††§§
= 0.80	6††¶¶
= 0.70	4††***
Assume that chelation therapy is given to all children with initial BLLs of 25 µg/dL and that chelation reduces their BLLs to 20 µg/dL after 1 year	10
Reduction in IQ per 1 µg/dL increase in BLL	
= 0.1	24
= .185[23]	17
= 0.5	9
Reduction in final grade attained for each increase in lead exposure sufficient to reduce IQ by one point	
= 0	21
= 0.2	12
Average lifetime earnings of a 1-year-old child discounted to the present	
= $200,000	16
= $500,000	9
Primary prevention benefit of reducing lead in housing	
= $0	17
= $2000	10

*Results are presented if changes in assumptions within the ranges presented in Tables 2-5 changed the threshold at which benefits first exceed costs by more than ±3% compared with the base model result of 14%. Changing the following variables resulted in changes of 3% compared with the base model: within-individual GSD; changes in children's BLLs from age 1 to age 2; direct medical and nonmedical costs of venipunctures, provider visits, educational interventions, environmental assessments, and courses of succimer or EDTA; risk of failure to graduate from high school because of increases in lead exposure; reductions in wages associated with IQ loss or final grade attained; or special education costs associated with lead exposure.
† 10 µg/dL.
‡These estimates overestimate the prevalence at which benefits would exceed costs because they assume no additional health or economic benefits of more expensive interventions.
§These additional costs could be offset (i.e., benefits would exceed costs at a prevalence of 14%) if the ratio of BLLs after the intervention to those that would otherwise have occurred was 0.96 for all children who had environmental interventions.
¶These additional costs could be offset (i.e., benefits would exceed costs at a prevalence of 14%) if the ratio of BLLs after the intervention to those that would otherwise have occurred was 0.88 for all children who had environmental interventions.
** These additional costs could be offset (i.e., benefits would exceed costs at a prevalence of 14%) if the ratio of BLLs after the intervention to those that would otherwise have occurred was 0.74 for all children who had environmental interventions.
††These additional costs could be offset (i.e., benefits would exceed costs at a prevalence of 14%) if the ratio of BLLs after the intervention to those that would otherwise have occurred was 0.40 for all children who had environmental interventions.
‡‡These estimates of prevalence at which benefits would exceed costs are probably too low because they are based on the assumption that more effective interventions could be done for no additional cost.
§§This additional benefit would be offset (i.e., benefits would exceed costs at a prevalence of 14%) if an intervention this effective cost at least $3218.
¶¶This additional benefit would be offset (i.e., benefits would exceed costs at a prevalence of 14%) if an intervention this effective cost at least $5468.
***This additional benefit would be offset (i.e., benefits would exceed costs at a prevalence of 14%) if an intervention this effective cost at least $8286.